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30 SEPTEMBER 1986

Japan Report

SCIENCE AND TECHNOLOGY

FBIS FOREIGN BROADCAST INFORMATION SERVICE

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BIOTECHNOLOGY

IMPACT OF RECENT DEVELOPMENTS ON INDUSTRIES DESCRIBED

Tokyo TOSHI KEIZAI in Japanese Nov 85 pp 10-30

[Excerpts] From a Dream Technology to a Practical Technological Era

Electronics and biotechnology, which is aimed at utilizing the functions of organisms for industrial purposes, are said to represent the "two major technological revolutions of the present century." As a key technology which will guide Japan through the 21st century, high hopes are being placed on biotechnology.

Among those countries engaged in biotechnological research, Japan has high expectations and aims to become a world leader. So far, brisk research has been conducted by both state and private-sector research institutions. As a result of this effort, Japan has established the basic techniques in its biotechnological research, including the techniques for gene recombination. As regards the development and application of biotechnology at the corporate level, most industry observers think Japan has almost caught up with the United States.

Because Japan is a country with scarce natural resources, high hopes are placed on biotechnology.

This is because of prospects that biotechnology can be applied to wide fields ranging from medicines, agricultural chemicals, foodstuffs, and industrial chemicals to agriculture, forestry and fisheries. In addition to these, application also extends to the generation of various resources and energy and to the field of electronics for the development of biotechnology-based sensors. Biotechnology is expected to have a significant impact on these industries in the future. There are estimates that in the year 2000, the market size of biotechnology-related industries may grow to ¥15 trillion, accounting for about 1 percent of the nation's gross national product (GNP) for the year.

These encouraging prospects cause people to place high expectations on the future of biotechnology. In the nation's stock exchanges, these bright prospects of the production of new materials which through biotechnology are reflected in substantial rises in stock prices of biotechnology-related businesses in recent years.

At present, biotechnology in Japan is moving out of the laboratory stage and is beginning to be used in practical applications on a commercial basis. With this recent progress in biotechnological R&D in Japan, the country has now entered a phase where coming trends and developments in the practical applications of biotechnology to various fields of the nation's industry must be watched closely.

In the pharmaceutical field, more than 100 companies in the country are engaged in biotechnological R&D. Their research includes an attempt to produce peptide in volume by means of gene recombination techniques. Peptide is a substance which exists within the human body in very small quantities and is an effective element for making medicines. Interferon is one of the products which have been created using biotechnology. The first interferon product has already been marketed on a commercial basis in Japan.

The application of biotechnology to practical purposes is not confined to the pharmaceutical field. A number of products which have been produced using biotechnology have already appeared on the Japanese market in the fields of food items, agricultural chemicals, and other industrial chemical goods. A detailed discussion on the progress of biotechnological R&D in these fields in the country will be given in later sections of this article. These days, the R&D activities in the biotechnology industry is gaining increasing momentum.

R&D in biotechnology in Japan in the recent past has been progressing at a faster pace than industry people originally visualized. The main driving force behind this rapid progress is believed to be the fierce competition among the world's industrially advanced nations in the race to develop high technology, which encourages R&D activities in the nation's biotechnology industry.

Competition among Japan, the United States, and Western European countries is particularly fierce. The stepped-up activities resulting from this strong rivalry support the prospect of Japan's biotechnology-related market increasing to ¥15 trillion in the year 2000.

In regard to future developments in Japan's biotechnological industry, two questions are: what direction industry will take in putting biotechnology into practical application and the market size of each application. Our observations on these questions are based on a forecast made by the Bioindustrial Development Center (BIDEC) of the Japanese Association of Industrial Fermentation.

In the coming 15 years by 2000, biotechnology is expected to be introduced for practical applications in the following fields:

Agricultural, Forestry, and Fisheries:

(In the following, A denotes the rate of possibility of realization of practical application of more than 80 percent, B more than 50 percent, and C higher than 20 percent.)

A. Development of hybrid species of rice, wheat, and vegetables. Cultivation of the tissues of seeds, saplings and flowering plants, and the production of useful substances in quantities from cultivation of these plants. An increase in the productivity of calves. An improvement of fish breeds.

B. Breeding of stools of vegetables for harvesting the seeds. Breeding of medicinal plants through cell fusion. Breeding of pearl oysters and seaweed.

C. Breeding of vegetables through cell fusion. Breeding of fruits.

Foodstuffs

A. Development of bread yeast. An improvement of wine yeast. Continuous fermentation of soysauce and liquors. Aspartame. Fermented proteins.

B. An improvement in efficiency in process for producing cornstarch. Lactase-fixing process in the production of milk having low milk sugar content. Rennet-fixing process in the production of cheese.

Industrial Chemicals

A. Biomass alcohols. Biomass chained-type intermediates. Biomembrane for gas separation. Production of materials for manufacturing dyes and spices from natural plants. Introduction of bioreactor techniques in the production of fine chemical products.

B. Production of ammonia from wastes resulting from amino acid production process. Introduction of bioreactor techniques into production of bulk chemical products. Use of lignin as the material for aromatic-family products.

Medicines

A. Insulin, human growth hormone, urokinase, TPA, somatostatin, endorphin, albumin, interferon, interleukin 2, TNF, CBF, MIF, EPO, prostaglindin, lectin, EPA, peptide-based medicines like (Mutostin), vaccines (hepatitis, influenza, polio), diagnostic medicines based on monoclonal antibody, microorganism-based antibiotic for sterilization.

B. Highly functional physiological activation substances.

Agricultural Chemicals

A. Microorganism-based chemicals.

B. Highly functional, safe agricultural chemicals.

Resources and Energy

A. (Bacterioleeching). Methane production from wastes. Hydrogen generation by use of microorganisms. Turning sewage water into industrially usable water.

B. Removal of harmful elements from industrial and other wastes.

Electronics and Machinery

A. Biotechnology-based sensors, artificial human body organs.

B. Biotechnology-based chips.

As far as the items listed above are concerned, those which have more than an 80 percent rate of possibility of realization are numerous. The coming 10 years starting in 1985 can be regarded as the decade in which the first full-fledged practical applications of biotechnologies will take place in various areas of the nation's industry and other fields.

The list on the next page shows the estimated market size of biotechnology businesses in eight major categories in 2000. Among those categories, medical goods are at the top of the list in the degree to which biotechnology will contribute to achievement of the estimated market growth figures. As far as the figures in the table are concerned, the contribution rate is 40 percent in the production of medical items followed by 30 percent in agricultural chemicals, 24.3 percent in the livestock business, 22.7 percent in food production, and 16.4 percent in fine chemicals. It is almost certain that in those fields the introduction of biotechnology will encourage a significant change in industrial structures in the future.

In achieving the estimated overall market size in the nation's biotechnology market in 2000, food, medical goods, agricultural products, and basic chemical goods manufacturing industries, as well as environment-related industry, will play central roles in attaining the estimated growth figures.

In the coming years, the difference in corporate strength among Japan's biotechnological companies may widen depending on each company's ways of tackling the efforts for practical applications of biotechnology.

In discussing the questions of practical applications of biotechnology, it will be necessary for us to take into account a number of different factors involved in the application process. There may be differences in the ways of putting the technology into practical applications and this will result in differences in the impact the application may have on the industries concerned.

There are three different conceivable patterns which must be taken into account in putting biotechnology into practical applications.

The first of these patterns concerns the commercialization of the products which are manufactured using biotechnology, and this is called product innovation.

The second pattern can be called process innovation and involves conversion from conventional production processes to biotechnological process in manufacturing. The third pattern concerns the market demand which would be newly induced by the introduction of biotechnology.

[Table] Size of Biotechnology Markets in Japan in 2000

Industries	Fields	Markets	Shares of biotechnology in percent of market output by field	Market sizes of biotechnology by field	Ratios in percent against aggregate total output of industries in Japan
		¥100 million		¥100 million	
Agriculture, forestry, and fisheries	Sizes of Agriculture	116,656	12.0	14,014	9.0
	Livestock	19,593	24.3	4,757	3.0
	Forestry	12,890	0.7	85	0.1
	Fisheries	39,778	3.0	1,181	0.8
	Total	188,917	10.6	20,037	12.9
Food	--	187,079	22.7	42,473	27.2
Paper pulp	--	17,970	5.0	899	0.6
Chemicals	Basic chemical products	128,313	11.9	15,221	9.8
	Fine chemicals	65,751	16.4	10,761	6.9
	Total	194,066	13.4	25,982	16.7
Medical and agricultural chemicals	Pharmaceuticals	78,785	40.0	31,514	20.0
	Agricultural chemicals	4,720	30.0	1,416	0.9
	Total	83,505	39.4	32,930	21.1
Resources, energy, and environment	Resources	54,374	6.2	3,345	2.1
	Energy	280,461	1.7	4,628	3.0
	Environment	85,988	15.9	13,702	8.8
	Total	420,823	5.0	21,675	13.9
Electronic equipment and machinery	--	179,114	3.4	6,035	3.9
Supporting of biotechnology R&D	Test equipment and chemical reagents	6,000	--	6,000	3.8
Grand total		1,277,478	12.2	156,031	100

Generally speaking, the application of biotechnology for producing medical goods and agricultural-related items could belong to the first pattern. Those belonging to the second pattern are food as well as chemical-related applications. Those coming under the category of the third pattern are experimental equipment and chemical reagents for example.

But when other, more detailed, factors pertaining to those items classified under the three patterns are taken into consideration, the outcome would become a little different from the generalized method of classification given above. When a new factor is taken into account, there may be a number of items in which those three patterns coexist.

For example, in the field of medical goods, urokinase, which is already produced using biotechnology on a commercial basis, is a product which belongs to the second pattern. But some physiological activation substances, another of the medical items now under development using biotechnology, belong to the first pattern.

Among the three patterns, the third is induced by the interplay of the other two and because of this we will drop the third from our discussion. For a company, quite different impacts result from product innovation as represented by the first pattern and from the second pattern, process innovation.

The first pattern involves delivering a new product to the market, and this would be of significance to the company in that the product may help the firm expand the markets for its products.

In contrast to this, the main aim of process innovation is to try to reduce the production costs of the firm's existing commercial items by innovating the manufacturing process, and the innovation will not, necessarily, enable the company to develop a new market in addition to the market for the existing products.

In this sense, the benefits the company would gain by process innovation are smaller than those resulting from product innnovation. But from the point of view of the competitiveness of a corporation, it can be said that the second pattern factor has significant importance.

However, generally speaking, in evaluating the values of stocks of a business corporation, people tend to attach greater importance to the first pattern factor, product innovation, rather than to the second, process innovation.

Before concluding this chapter, we will touch on what benefits the involvement in biotechnology may bring to those companies which are pushing ahead their R&D in an effort to put the technology into practical application.

As described in the preceding passages of this chapter, the application of biotechnologies to commercial purposes will result in the supply of new biotechnology-based products to the market and an improvement in efficiency in the production process.

To sum up, the effects brought about by the introduction of biotechnology into the nation's industry will help industry manufacture products with a higher value added to them.

As a typical example, there is the beta-type interferon which was developed by Toray Industries, Inc., headquartered in Tokyo. The interferon has fetched an extraordinarily high retail price as a medicine.

According to investigations conducted by BIDEC, the degree of value added to products which were made using biotechnology stood at 43 percent. This compares with 36 percent for the products manufactured using conventional production technology. Consequently, the manufacturers of biotechnology-based products could make more money and this will contribute to an improvement in their corporate strength.

Another important point which must be noted in the biotechnology business is that considering the broadly based foundation of biotechnological R&D activities in terms of the technologies involved, continued R&D in the coming years will make it possible for the technology to be applied to a wide field of industry in the future.

This prospect has already been clear in a phenomenon of the recent past in which many domestic companies representing various industries, such as food products and chemical goods makers, are entering the booming medical products markets one after another armed with biotechnology.

This phenomenon has led to a lowering of barriers between different industries in the nation. At the same time, this lowering of barriers has proved beneficial to corporations in that it has given them an increased chance to stay in business by diversifying their business lines.

The negative side of lowering barriers is the collapse of the long-standing corporate orders in the nation's industry leading to increased competition among companies. The increased competition may further aggravate the differences in corporate strength among the nation's companies in the future.

In the following chapters, we will report on the progress in R&D of biotechnology in five different fields of the nation's industry--medical goods, seeds, and saplings, foodstuffs, agricultural chemicals, and other industrial chemical products. Differences are already apparent among those five separate groups.

Food Field: Industrialization Advances on Bioreactor

Scale of ¥6 Trillion in 21st Century--Driving Key Technology Extensively

Bio Market at Greatest Scale

It is almost certain that biotechnology, along with electronics, will continue to attract much attention as revolutionary key technologies over the coming period extending toward the turn of the century. According to calculations conducted by the Bioindustrial Development Center (BIDEC) of the Japanese

Association of Industrial Fermentation, the nation's biotechnology markets are expected to grow to ¥15 trillion by 2000. Of this figure, the largest share, 41 percent, is expected to be taken by food-related industries--¥6.25 trillion by the agricultural, forestry, and fisheries industries and ¥500 billion by the food manufacturing industry. They will be followed by the medicinal and agricultural chemical manufacturing industries (¥3.29 trillion in total with a combined market share of 22 percent), and industries producing other industrial chemical products (¥2.6 trillion, 17 percent).

Following are some examples of R&D being conducted in the food-related industries in applying biotechnologies. Nichirel Corp. is engaged in raising "pomato," a new agricultural crop which has been created by fusing the cells of the tomato and the potato. Kikkoman Corp. is conducting research on cell fusion between the ordinary orange and the trifoliate orange. The Agriculture, Forestry, and Fisheries Ministry's experimental stations are conducting research on growing the protoplast of rice plants. The ministry, in a joint research effort with three private-sector dairy product and and animal feed firms--Snow Brand Milk Products Co., Ltd., Chubu Shiryo Co., Ltd., and Meiji Milk Products Co., Ltd.--is also engaged in producing calves using the techniques of transplantation of split fertilized eggs. In addition, efforts are being made to apply biotechnologies involving the use of enzymes and enzyme-fixation techniques to developing such electronics devices as sensors and chips. Some of these biotechnology sensors are already used in practical applications. One such sensor is developed for measuring the freshness of fish. The sensor makes use of the electrical phenomena occuring on the body of a fish. The sensor's mechanism makes it possible to realize efficient exchanges of the electrical energy involved and an efficient transmission of the information from the body of the fish to the measuring instrument. The ultimate goal of the research involving sensors and chips is to create a "biocomputer" which operates by imitating the function of the human brain. The computer is expected to process a huge volume of information, store it, and generate no heat. The basic research for creating such a computer is already underway.

It is expected that completing a biocomputer will take many years. Concrete results toward making the first model of a biocomputer are likely to be achieved by 2000.

In the field of agricultural industry, according to BIDEC, the fruits of biotechnology research will first be applied to such crops as rice, wheat, vegetables, fruits and potato. The organization expects that increased efficiency in breeding resulting from a combination of the traditional crossing techniques and new tissue cultivation techniques will lead to the development of FI species, increased productivity and the development of new species resisting crop diseases better. The development of new types of crops through cell fusion and gene recombination techniques has succeeded in some kinds of crops. In addition to these developments, it is expected that future progress in the application of biotechnology in the agricultural area will be made in growing saplings and flowering plants and the production of medicinal plants through tissue cultivation techniques. In the livestock industry, progress may also be achieved in the manipulation to promote ovulation of multiple eggs,

increasing productivity of calves through the transplantation of multiple numbers of fertilized eggs, and in increasing milk production through the introduction of highly productive species of milch cows. Progress could also be forthcoming in the basic research on the transplantation of the split egg embryo and nuclear transplantation. In the field of fisheries, there are a number of instances where biotechnological research has progressed to the point where the technology can be put to practical use. They include the breeding of new female species through chromosome manipulation and the breeding of other marine creatures through doubling of chromosome numbers. Research on the cultivation of tissues of pearl oysters and seaweed and cell fusion may also advance in the coming years.

Turning to the food manufacturing industry, favorable results are expected to be made in the fields of dairy products, bread, candies, sugar, seasoning, starch, starch syrup, grape sugar, assorted feed, and liquors. This prospect has increased due to the progress made so far in basic research on the introduction of new bacteria created through gene manipulation into the food-manufacturing process and also due to the progress achieved in continuous fermentation through fixation in applying fermentation technology to practical purposes. Based on such progress, the nation's food-related industries expect their biotechnological product makers will grow to ¥6.25 trillion by 2000. The growth figure breaks down into ¥2 trillion in agricultural, forestry, and fisheries industries, and ¥2.5 trillion in food manufacturing industry. [Figures as published]

Until recently, the biotechnological industry in Japan has been exploiting the benefits accruing from biotechnological R&D efforts by simply using enzymes and bacteria without trying to unravel their physiological functions. However, recent trends in the biotechnology industry in the country point toward trying to exploit more positively the physiological functions of those enzymes and bacteria by trying to unravel scientifically the mechanism of their useful functions.

To promote this effort, there are four key technologies available: gene recombination, cell fusion, volume cultivation of cells, and bioreactor techniques. By organically combining these technologies, it becomes possible to use biotechnology effectively in applications in various fields of industry.

Gene Recombination

Gene recombination is a technique to artificially transplant a necessary part or piece of information of the DNA or gene of one living thing to another living organism to create a new living thing having the needed characteristics and functions.

The gene splicing technique developed by Kikkoman Corp. is an epoch-making method. It utilizes a virus called bacteriophage as carriers of the gene instead of using an extranuclear gene, a genetic substance which does not belong to the chromosome. In the Kikkoman method, the number of the bacteriophage increases with the multiplication of the host. When a thermal shock is

applied after the multiplication in the host is sufficient, the bacteriophage promptly duplicate themselves within the host. This phenomenon allows the production of a far larger volume of useful substances than using an extra-nuclear gene. The Kikkoman method allows control of the production volume of useful substances by adjusting the thermal stimulation making it easier to apply the method to practical industrial applications.

On the other hand, in joint research with the Agriculture School of the University of Tokyo, Kirin Brewery Co., Ltd. has discovered that the mitochondrial DNA in the cytoplasm of rice is responsible for a phenomenon in which pollen is not produced, preventing rice from bearing seeds. This finding of the company drew the attention of the agriculture industry because the finding has opened the way for developing F1 species of rice by gene recombination.

Cell Fusion

Cell fusion calls for artificially combining the cells of two different kinds of plants through fusion, not through ordinary crossing, to create a useful new cell which combines the functions and characteristics of the two separate plant cells.

When the cells involved in the fusion are animal cells, Sendai virus is used as an agent to promote the fusion process, while in the case of plant cells, polyethylene glycol is employed as the promotional agent. In the case of plant cells, preparatory processing is required to remove the hard cell walls, which protect the protoplast, using special enzymes prior to implementing the fusion. Kirin Brewery Co., Ltd. uses zymolyase as the cell wall dissolving enzyme, while Kikkoman Corp. uses pectolyase Y23 for the purpose.

A number of companies are currently engaged in brisk research in the field of plant breeding. Nichirei Corp. has stepped up research at its subsidiary on pomato, a fusion of the cells of a tomato and a potato. Prof Johann Georg Friedrich Melchers, an internationally renowned specialist on cell fusion from West Germany, has been invited to participate. The subsidiary, Agrogenetic Co., capitalized at ¥5 million, was set up in May 1984, and Nichirei controls 78 percent of the assets of the research subsidiary. The aim of developing the pomato is to create a new variety of tomato which has as good winter-hardy characteristic as the potato. The research to enable the pomato to bear fruit has made some gains in the recent past and this progress has made it possible for Nichirei to put the techniques involved in creating the pomato into practical use in the near future.

Another company, Kikkoman Corp., has been engaged in a cell fusion research project involving the trifoliate orange and the trovita orange, both belonging to the orange family, with the Agriculture, Forestry, and Fisheries Ministry to improve the plants. The company has already succeeded in the cell fusion and the fused cells have now grown into saplings. The imporant thing in the cultivation of fused cells is the development of a special cultivation medium which contains the growth hormone, and the development of another medium in which only the fused cells can selectively grow. The success in fusing the

cells of the two orange family trees means that Kikkoman has taken a big step forward toward creating a variety of orange tree which has a good winter-hardy characteristic. This success has increased the possibility of successfully applying the fusion techniques to such cereals as rice and wheat in the future. In rice and wheat, the differentiation and reconstruction of the cells are difficult.

Yet another company, Japan Tobacco Inc., has succeeded in the fusion of cells of a wild tomato with those of the cultivated species. The newly created species has increased fertility characteristics. This is the first time in the world that a new species of tomato has been developed. The corporation has been conducting the fusion research for the Ministry of Agriculture, Forestry, and Fisheries.

Volume Cultivation of Cells

The technology involved in the volume cultivation of plant cells is important to realize mass production of the cells of a new plant by promoting the multiplication of plant cells which have been created either through gene recombination or cell fusion. Under the presently available technology, in cultivating animal cells, use of the cultivation medium based on costly blood serum of cow embryos is indispensable. A problem with using the serum-based medium is the low cultivation densities of the cells. In search for breakthroughs to this problem, research has been conducted in Japan for a new cultivation method which does not require the use of the blood serum of cow embryos and will allow higher densities of the cell cultivation.

Nichirei Corp.'s subsidiary UBC and Koboko's subsidiary (Gibco) Oriental are importing the media from the United States and marketing it in Japan. In addition to these firms, Nippon Suisan Kaisha, Ltd., is also marketing its own product through its subsidiary Nissui Seiyaku. Nichirei Corp. is developing a new cultivation medium containing lower content blood serum of cow embryos with the Agricultural School of Kyushu University. Besides these, a number of other companies related to biotechnology are engaged in research to develop cultivation methods in the fields of plant breeding and the production of medicines. Those companies include the aforementioned Kikkoman Corp., which is conducting research on cell fusion of plants.

Examples of cultivation media, are red pigment anthocyanin by Nippon Paint Co., Ltd., ginseng by Nitto Electric Industrial Co., Ltd., shikonin by Mitsui Petrochemical Industries, Ltd., peroxidase by Toyobo Co., Ltd., and gold-banded lily by Kyowa Hakko Kogyo Co., Ltd.

Bioreactor

Bioreactor is a technology which makes industrial use of various chemical reactions occurring inside a living body outside of it. Enzymes and bacteria are being utilized as catalysts to promote the chemical reactions. The bioreactor techniques allow production of only what is needed under ordinary temperature and atmospheric pressure conditions. Companies which have succeeded in putting the bioreactor techniques into industrial use are Tanabe

Biotechnology R&D by Food and Beverage Makers

Company names	Remarks
Showa Sangyo Co., Ltd.	Engaged in biotechnological business by producing high fructose syrup. Participating in a biotechnology project sponsored by the Ministry of Agriculture, Forestry, and Fisheries.
Morinaga & Co., Ltd.	Established the Morinaga Biochemical Research Lab in 1981. Has achieved progress in research involving cell fusion and monoclonal antibody.
Meiji Seika Kaisha, Ltd.	Engaged in the development of a number of new pharmaceutical products. The market for the firm's biotechnological herbicide, Herbiace, is growing.
Meiji Milk Products Co., Ltd.	Has marketed a number of types of monoclonal antibodies. Has succeeded in gene recombination of lactic acid bacteria for the first time in the world.
Snow Brand Milk Products Co., Ltd.	Has top-notch ability in fertilization of cow's ovum, implantation of the fertilized ovum, splitting and preservation of the ovum. Engaged in breeding of plants through the firm's subsidiaries.
Sapporo Breweries, Ltd.	Making efforts to discover new useful substances using antinomycetes. Engaged in breeding of plants. Also conducting research on bioreactor technology.
Kirin Brewery Co., Ltd.	In the field of plant breeding, succeeded in developing a new species of barley for brewing beer which the firm named Amagi Nijo. Actively engaged in biotechnological research involving cell fusion and gene recombination.
Takara Shuzo Co., Ltd.	Has made a great contribution to the progress of biotechnological research through research involving synthetic DNA, DNA synthetase and a restriction enzyme as a reagent for use in genetic engineering.
Nada Jozo Co., Ltd.	Draws industry attention after it has been reported that Asahi Chemical Industry Co., Ltd., intends to sell TNF, a pharmaceutical product under development by the firm, through the marketing channel of Nada Jozo.
The Calpis Food Industry Co., Ltd.	Has succeeded in unraveling the mechanism of the working of a gene responsible for dumping what is produced within the bodies of bacteria outside of the bodies in a gene recombination process.
Kikkoman Corp.	Engaged in breeding of plants, including tomato. Has succeeded in cell fusion experiments. Has achieved progress in bioreactor R&D.

[continued]

[Continuation of Biotechnology R&D by Food and Beverage Makers]

Company names	Remarks
Ajinomoto Co., Inc.	Engaged in the development of Interleukin II and III, and blood substitute.
Nichirei Corp.	Has achieved progress in research involving a monoclonal antibody. Maintains close relations with Dr Johann Georg Friedrich Melchers, a West German international expert in cell fusion research.

Seiyaku Co., Ltd., which manufactures amino acids, and Showa Sangyo Co., Ltd., and Japan Maize Products Co., Ltd., which produce isomerized sugar. In addition to these private-sector companies, governmental institutions are also engaged in active R&D activities making use of bioreactor techniques. The Ministry of International Trade and Industry's fuel oil development laboratory (RAPADO), as well as the ministry's new energy development organization (NEDO), and conducting research to develop the technology for producing fuel alcohol. The Ministry of Agriculture, Forestry, and Fisheries is pushing ahead with research to develop bioreactor systems for application in the food manufacturing industry.

The RAPADO program is being participated in by two separate groups of private-sector firms. One group has as members Kyowa Hakko Kogyo Co., Ltd., Kurita Water Industries, Ltd., and Toyo Engineering Corp. The other group consists of Nikki Chemical Co., Ltd., Sanraku-Ocean Co., Ltd., Ajinomoto Co., Inc., Kansai Paint Co., Ltd., and Maruzen Oil Co., Ltd. The research by these two groups has made progress to the point that the results of the research can be put into practical application in the very near future. On the other hand, NEDO's research program is participated in by Kirin Brewery Co., Ltd., Takara Shuzo Co., Ltd., Sanraku-Ocean Co., Ltd., Suntory Ltd., Kansai Paint Co., Ltd., Nikki Chemical Co., Ltd., and Hitachi Shipbuilding & Engineering Co., Ltd. Their research involves the use of syrup and cellulose as materials.

Medical Supplies: "The Dream New Medicine" on Timetable

New Bio-Medicine Encountering Blooming Period--First Interferon No 1, Emerges

Medical Supplies Lead VAN in Commercialization

About 10 years have elapsed since the present biotechnology involving gene recombination as part of the technology was born. Medicines are the first item which embody the progress achieved in biotechnological research over the past years in the form of a commercial product.

Several reasons can be pointed out for medical products becoming the first to appear on the commercial market. First, medicines are a product having high added values. This enables the developers of medicine to recover relatively

easily the money which they invested to develop the medicine, whatever large sums of money they invest. A second reason concerns the technical aspects involved. Interferon and insulin can be manufactured effectively by introducing a certain useful type of gene into the host for their production only when such a gene was discovered. A third reason is that the development and production of new useful medicines meet the interests not only of the pharmaceutical firms, but also of society.

Relationships between the development of medicines and biotechnology involving the use of the cells and tissue of living organisms as research materials date back many years. Antibiotics developed using bacteria are an example of products resulting from such a relationship. As exemplified in antibiotics, it can be said that inseparable relationships have existed between them from the beginning. At the same time, it can also be said that their continued relationship will bring us further benefits in the future.

At present, two kinds of biotechnological medicines are being marketed, and both have been developed by Japanese companies. One is a thrombus dissolvent, urokinase, which was put on the market in June 1984. The blood clot dissolving agent was jointly developed by four firms--Dainippon Pharmaceutical Co., Ltd., Dainabot Co., Ltd., Kyorin Pharmaceutical Co., Ltd., and Mitsubishi Yuka Fine Chemicals Co., Ltd. Another is a cancer-fighting drug, beta interferon, which was marketed in August 1985. The medicine was developed by Toray Industries, Inc., and is marketed by Daiichi Seiyaku Co., Ltd.

As a blood clot dissolving medicine, the urokinase extracted from human urine has been used until recently. But the newly marketed urokinase is based on the plasminogen activation enzyme. The new urokinase medicine was developed by Abbott Laboratories of the United States for the first time in the world using biotechnology and tissue cultivation techniques. In Japan, research to develop the enzyme was launched in 1971. The products produced using the technique have several advantages: good uniformity of the composing elements and a high specific dissolving power per unit of proteins. The technique allows the production of products having lesser degrees of biological impurities.

The anticancer beta interferon developed by Toray Industries using biotechnology and marketed by Daiichi Seiyaku, is trade-named Feron. The cancer-controlling drug was derived from human diploid cells. It is produced by cultivating human cells. The beta-type interferon is obtained by applying an interferon-inducing agent to the cultivated cells. The production process is as follows: First, the human diploid cells (somatic cells) are made to multiply by being put on the surfaces of tiny glass balls with a diameter of about 0.15 mm and cultivated in the tanks of the production facility. Then certain different kinds of proteins are introduced into the multiplied cells to induce the formation of the beta-type interferon in the cells. The production process of the cancer-fighting drug is completed by refining the beta-type interferon thus produced and then freeze-drying. As a biotechnological medicine, the cancer-controlling drug can be regarded as a more genuine biotechnological medicine than the aforementioned urokinase.

Biotechnology Medicines and Firms Producing Them

Products	Product names and firms making them
Medicines for immunotherapy	Sankyo Co., Ltd./Kureha Chemical Industry Co., Ltd. (Krestin); Chugai Pharmaceutical Co., Ltd. (Picibanil); Yamanouchi Pharmaceutical Co., Ltd./Ajinomoto Co., Inc. (Lentinan: Government permission for production of this medicine has yet to come); Fujisawa Pharmaceutical Co., Ltd. (Rubratin: Government permission has yet to come); Nippon Kayaku Co., Ltd. (Ubestatin: Official permission has yet to come) Kureha Chemical Industry Co., Ltd. (K-18); Kaken Pharmaceutical Co., Ltd./Daito Chemical Industry Co., Ltd. (Sonifilan); Yakult Honsha Co., Ltd. (LC-9018); Sapporo Breweries Ltd./Daicel Chemical Industries, Ltd. (RBS); Kirin Brewery Co., Ltd. (ZYM, KS-2); Banyu Pharmaceutical Co., Ltd. (PRF); Kyowa Hakko Kogyo Co., Ltd. (Levamizole); Zerya Seiyaku Kogyo Co. (Maruyama vaccine); Takara Shuzo Co., Ltd. (PS-1426)
Interferon Interferon derivatives	There are three types of interferon: alpha type, beta type, and gamma type. Among these, gamma type is the most effective in controlling the multiplication of cancer cells. The firms producing interferon and the derivatives are: Toray Industries, Inc., Takeda Chemical Industries, Ltd., Sumitomo Chemical Co., Ltd., Mochida Pharmaceutical Co., Ltd., Yamanouchi Pharmaceutical Co., Ltd., Daiichi Seiyaku Co., Ltd., Shionogi & Co., Ltd., Kyowa Hakko Kogyo Co., Ltd., and Meiji Seika Kaisha, Ltd.
Lymphokine cytokinin	TNF: Dainippon Pharmaceutical Co., Ltd., and Asahi Chemical Industry Co., Ltd.; OH-1: Hayashibara Biochemical Laboratories, Inc. and Mochida Pharmaceutical Co., Ltd.; Lymphotoxin: Fujisawa Pharmaceutical Co., Ltd.; Interleukin: Ajinomoto Co., Inc., Kureha Chemical Industry Co., Ltd., Takeda Chemical Industries, Ltd., and Shionogi & Co., Ltd.; Prostaglandin: Ono Pharmaceutical Co., Ltd., Teijin Ltd., Taisho Pharmaceutical Co., Ltd., and Chugai Pharmaceutical Co., Ltd.; MIF: Denki Kagaku Kogyo K.K.
Monoclonal antibody	Teijin Ltd., Fujirebio Inc., Kureha Chemical Industry Co., Ltd., Asahi Chemical Industry Co., Ltd., Mitsubishi Chemical Industries, Ltd., Kirin Brewery Co., Ltd., Mitsubishi Yuka Fine Chemicals Co., Ltd., Meiji Milk Products Co., Ltd., and Meiji Seika Kaisha, Ltd.

R&D on Interferon for Cancer Treatment by Major Firms

Type	Firm names	Production methods	Suppliers of technology (original)
α	Sumitomo Chemical Co., Ltd.	Cell cultivation	Welcome Foundation
α	Takeda Chemical Industries, Ltd.	Gene recombination	Roche (Genentech)
α	Yamanouchi Pharmaceutical Co., Ltd.	Gene recombination	Schering
α	The Green Cross Corp.	Cell cultivation (derived from white blood corpuscle) Cell cultivation (derived from lymphoblast) Gene recombination	Developed on its own Developed in-house Developed in-house
α	Mochida Pharmaceutical Co., Ltd.	Multiplication of hamsters	Hayashibara Biochemical Laboratories, Inc.
β	Toray Industries, Inc.	Cell cultivation	Developed by the firm itself. Marketing is done by Daiichi Seiyaku Co., Ltd.
β	Toray Industries, Inc., Kyowa Hakko Kogyo Co., Ltd.	Gene recombination	Cancer Research Association
β	Mochida Pharmaceutical Co., Ltd.	Cell cultivation	G.D. Searle & Co.
γ	Meiji Seika	Gene recombination	G.D. Searle & Co.
γ	Toray Industries, Inc., Daiichi Seiyaku Co., Ltd.	Gene recombination	G.D. Searle & Co.
γ	Asahi Chemical Industry Co., Ltd.	Gene recombination	Developed on its own
γ	Kyowa Hakko Kogyo Co., Ltd.	Gene recombination	Cancer Research Association
γ	Takeda Chemical Industries, Ltd.	Gene recombination	Roche (Genentech)
γ	Shionogi & Co., Ltd.	Gene recombination	Biogen
γ	The Green Cross Corp.	Tissue cultivation Gene recombination	Technology developed by the firm itself Developed by the firm

Note: The white blood corpuscle derived interferon developed by Green Cross Corp. was filled by the company with the government as a medical product in the category of ophthalmology for permission to produce in May 1981.

After the Health and Welfare Ministry's permission to produce the beta interferon as a cancer fighting drug was secured for the first time in March 1985, the drug began to be marketed on the domestic market in August. The drug is said also to be effective in treating B-type hepatitus. Toray Industries, the developer of the drug, has filed an application with the ministry to have the effectiveness recognized. For the time being, before the extended effectiveness is officially recognized, the use of Toray's interferon-based drug will be restricted to treating brain tumors and skin cancer. The company expects the sales of the drug in the initial 1-year period to reach ¥2 to ¥3 billion.

Interferon, which is regarded as the first fullfledged biotechnological medicine in the country, has fetched high sales prices. The price is ¥23,791 per 1 million international units. In clinical application, the dosage of interferon administered to a patient at one time is 3 million international units, so this means the cost for a single dose of the medicine comes to more than ¥70,000. This fact of newly developed biotechnological medicines fetching high prices has worked to further encourage the nation's pharmaceutical firms to step up their research to develop new biotechnology drugs.

In fact, brisk efforts to develop new biotechnological drugs to follow beta interferon are underway in the nation's pharmaceutical industry. Among those drugs, particular emphasis is placed on the cancer medicines. Among those anticancer biotechnological drugs currently being used clinically are gamma interferon, interleukin 2, OH-1, and TNF.

Among those cancer drugs being tested clinically, the gamma interferon is expected to grow into a major cancer drug in the future. This prospect has prompted many companies to enter the market not only from the pharmaceutical industry, but also from food and textile industries. Already, seven separate groups of companies are involved in clinical tests of their products, aiming at putting them into practical applications in 3 or 4 years.

Among these groups, the most advanced is the group of Shionogi & Co., Ltd., and Biogen Co. In 1982, Shionogi introduced a volume production method of gamma interferon which involves the techniques of gene recombination of colon bacilli. In November 1983, the company began clinical tests of the interferon ahead of other competitors. The company is scheduled to file an application with the Health and Welfare Ministry for government permission early next year (1986) to start commercial production of the anticancer drug. Officials of Shionogi say: "We aim at being the first in commercializing (the interferon), too."

Immediately on the heels of the Shionogi-Biogen group are four groups of firms which form the bigger second cluster of firms together in the race to grab the new booming market. One of the principal firms in the cluster is the Green Cross Corp. A second group in the cluster companies Takeda Chemical Industries, Ltd., and Nippon Roche K.K. The third pair is Toray Industries, Inc., and Daiichi Seiyaku Co., Ltd., and the fourth entity in the cluster is Kyowa Hakko Kogyo Co., Ltd. All these companies began clinical tests of their

Major Biotechnology Medicine Makers and Their Activities

Firm names	Remarks
Asahi Chemical Industry Co., Ltd.	Pioneered in the R&D of tumor necrosis factor (human TNF) drug and the third generation product of blood clot dissolving agent TPA.
Dainippon Pharmaceutical Co., Ltd.	The firm was the first to develop a biotechnological drug. The firm is competing with Asahi Chemical Industry Co., Ltd., in the development of human TNF.
Sankyo Co., Ltd.	Has a business tieup with Celltech Ltd. of Great Britain in R&D of TPA and MAF. Expected to step up R&D in the future.
Yamanouchi Pharmaceutical Co., Ltd.	Started developing a TNF-like substance called KBS.
Shionogi & Co., Ltd.	Began clinical testing of IL-2 in February 1985. The firm runs ahead of other competitors in R&D of gamma IF.
Takeda Chemical Industries, Ltd.	Runs ahead of others in R&D of IL-2. Fast catching up with the frontrunner in gamma IF.
Sumitomo Chemical Co., Ltd.	Runs ahead of others in the Phase III of R&D of human growth hormone.
Green Cross Corp.	Displays diversified activities in R&D of IF.
Toray Industries, Inc.	Has achieved good results in R&D of a new, full-fledged biotechnological medicine called Feron. The medicine has been found also to be effective in treating patients suffering from B-type hepatitis.
Mitsubishi Chemical Industries, Ltd.	Displays diversified activities in R&D of new biotechnological medicines. It is the frontrunner in the development of TPA which the firm developed jointly with Kyowa Hakko Kogyo Co., Ltd.
Kirin Brewery Co., Ltd.	Has unraveled the structure of the genes of IL-2 for the first time in the world.
Fujisawa Pharmaceutical Co., Ltd.	Expected to begin clinical application of lymphotoxin from the spring of 1986.

products in the first half of 1984 and there are no significant differences among them in the degree of progress in their R&D activities.

However, among these companies, the Green Cross Corp. is the only firm which employs a unique method of producing interferon. The company's method calls for the cultivation of human white blood corpuscles to produce the gamma interferon. The other companies employ a different method in which the colon bacilli are cultivated in volume after a gene recombination process to produce the interferon.

Among the third cluster of companies trailing the second are Suntory Ltd. and Meiji Seika Kaisha, Ltd. Both companies began clinical tests of their products in the spring of 1985 and aim to catch up with the top group. As described thus far, all of these companies engaged in the production of the gamma interferon are expected to be able to put their products into practical application in the near future.

Another biotechnological medical product which is competing with gamma interferon to be the first commercially produced cancer-fighting drug is human TNF. Two domestic companies are competing to develop the human TNF. They are Asahi Chemical Industry Co., Ltd., and Dainippon Pharmaceutical Co., Ltd. Asahi Chemical has established the technology for producing the TNF in volume using gene recombination techniques in joint research with the City of Hope Research Institute of the United States. Asahi Chemical has been conducting clinical tests of the cancer drug since April 1985 ahead of competing companies. The company has obtained good results in the phase-I test of the drug and is going to enter phase II in October (1985). The firm has been carrying out clinical tests not only within Japan, but also in a number of foreign countries. Asahi Chemical said it believed the company could secure permission in Europe to start manufacturing the human TNF there in 2 years' time at the earliest.

Dainippon Pharmaceutical is the strongest competitor of Asahi Chemical in the race to develop the anticancer drug. Dainippon Pharmaceutical began conducting clinical tests of rabbit TNF in November 1984. Following this, the company began the clinical testing of human TNF which the firm developed using gene recombination techniques in May 1985. In the middle of September the same year, the company notified the Health and Welfare Ministry that it was going to enter phase II in the clinical tests of the anticancer drug. Starting late that month, the company was going to start investigating the effectiveness and safety of the human TNF by administering the drug to cancer patients at more than 10 hospitals, centering on those located in the Kansai region in western Japan. The on-going competition between Dainippon Pharmaceutical and Asahi Chemical is literally a nip-and-tuck race.

TNF is a physiological activation substance present within the human body. It has the ability to distinguish between normal cells and cancerous cells. (When used in anticancer drugs,) the TNF has the characteristics of attacking only cancerous cells to destroy them. Because of this, human TNF is regarded as the most effective anticancer drug in the world. In addition to Asahi Chemical and Dainippon Pharmaceutical, Fujisawa Pharmaceutical Co., Ltd., and

Yamanouchi Pharmaceutical Co., Ltd. are also engaged in the development of similar cancer drugs and plan to start clinical tests in the near future.

Other than those anticancer drugs discussed thus far, OH-1 and physiological activation substance interleukin 2 are new biotechnological drugs which have been found to have cancer-controlling abilities. The companies involved in the development of interleukin 2 include Takeda Chemical Industries, Ltd., and Shionogi & Co., Ltd., group; Biogen Co., Ltd., and Ajinomoto Co., Inc. group; Yoshitomi Pharmaceutical Industries, Ltd., and the Cancer Institute group; and a cluster of companies comprising Genex, Suntory, Ltd., Green Cross Corp., Inc., Otsuka Pharmaceutical Co., Ltd., Toray Industries, Inc., and Hayashibara Biochemical Laboratories, Inc. OH-1's development is carried out by the Hayashibara Biochemical Laboratories and Mochida Pharmaceutical Co., Ltd. Interleukin is immune proteins present within the human body in very small quantities produced by the lymphoid cells. Interleukin is said to be an effective medicine to treat patients of AIDS (Acquired Immune Deficiency Syndrome) which is claiming the lives of an increasing number of people in foreign countries, centering on the United States. In view of the possible usefulness, interleukin is drawing much attention in the medical industry recently. In R&D of interleukin, Japan is the most advanced country in the world. Among domestic companies involved in the development of interleukin, Takeda Chemical Industries leads other companies. At present, the company is in the phase II stage of its development of the interleukin-based anticancer drug. In second position in the race to develop the interleukin drug is Shionogi & Co. which began the clinical evaluation of its product in February this year (1985).

Efforts to develop new biotechnological medicines are not confined to the development of anticancer drugs. Among other new biotechnological medicine candidates are TPA (human tissue plasminogen activator), a new type of blood clot dissolvent which would become the third generation of urokinase, human blood serum albumin, hepatitus vaccine, human growth hormone, and insulin as a medicine for the treatment of diabetes. In fact, many new biotechnological medicines are under development.

All of the base substances contained in these new biotechnological medicines under development exist in the human body in very small quantities. Until recently, it has been impossible to secure them in volume so they can be used to produce medicines. But the rapid progress in biotechnological research in recent years has made it possible now to obtain the substances in quantities. Now many of those new biotechnological medicines can be manufactured on a commercial basis soon.

According to the Bioindustrial Development Center (BIDEC) of the Japanese Association of Industrial Fermentation, the production value of pharmaceutical products in the nation in 2000 is expected to register about a 2.3 times increase, going up from the 1984 market size of ¥4.3 trillion to about ¥9.9 trillion. Of this estimated production value, biotechnological medicines are expected to account for 40 percent, reaching about ¥4 trillion. This market forecast is contained in BIDEC's report entitled "The Impact of Biotechnology on Industries in 2000."

Seeds/Plants: Enthusiastic Views on Seed Business

Expand Storage Capacity of "Seeds Bank"--Sudden Increase in Industries Entering Seed Business

Ministry of Agriculture, Forestries, and Fisheries Also Reinforcing Support System

The Agriculture, Forestry, and Fisheries Ministry has recently stepped up its efforts to promote R&D on biotechnology in the nation.

This is apparent in the opening of a biotechnology office (at the ministry) in April 1984, establishment of several technological research cooperatives, and a drastic increase in the capacity of plant seed storage facilities for the preservation of genetic resources (seed bank).

The major reason behind this move seems to be the ministry's perception of the need for Japan to try to increase the productivity of agricultural products to compete with U.S. products in the face of the recent U.S. demand for Japan to open its markets wider to American agricultural goods. Of course, there may be other reasons. First, the ministry's perception that it lags behind the Ministry of International Trade and Industry in high technology research fields, even though the Agriculture, Forestry, and Fisheries Ministry has been accumulating a huge volume of technologies in the fields of animal and plant research. The second reason is the ministry's perception that the technological levels in Japan for producing agricultural seeds lag behind that of foreign countries, particularly in the categories of major crops. The third reason may have something to do with the contents of the report on administrative reform submitted to Prime Minister Yasuhiro Nakasone by a governmental advisory council in which the council urged the deregulation of the seed market of principal agricultural crops.

The positive efforts made so far by the Agriculture, Forestry, and Fisheries Ministry to promote research on biotechnology in agricultural fields are represented by the ministry's assistance in the form of increased budgetary allocations, making available ministry-held resources for seed production to private-sector institutions and increasing the resources of the seed banks. Namely, the ministry has been stepping up its effort to promote biotechnological research in the country by extending monetary and material support.

Regarding the ministry's budgetary appropriations for biotechnology research, ¥1.278 trillion was earmarked in fiscal 1984, representing a 91 percent gain over the preceding year. In fiscal 1985, a 53 percent increase was made to ¥1.96 trillion over the previous year. For fiscal 1986, beginning on 1 April 1986, the ministry requests a budgetary appropriation for biotechnology research of ¥3.736 trillion, about double the 1985 figure.

Besides this budgetary allocation, the Agriculture, Forestry, and Fisheries Ministry has requested ¥5 billion from the government's industrial investment special account as funds to establish a center to promote the development of new agricultural, forestry, and fishery technologies. The ministry is now

aiming at briskly promoting the development and dissemination of biotechnology as well as other high technologies. Strengthening cooperation in these endeavors among government, industry, and academic research institutions is the ministry's long-term project which sets its target in the 21st century.

In addition, to establish a research system which the ministry hopes will allow close cooperation between the government and private-sector research organizations, the ministry will offer ministry-held seed resources for utilization by private-sector researchers. The ministry will also increase the number of items stocked at the seed bank from the current 50,000 to 150,000. At the same time, the ministry intends to centrally manage the seeds of agricultural crops and other plants, which at present are held by various institutions across the country. Generally speaking, Japan is behind some other foreign countries in the number of stocked genetic resources in agricultural and forestry fields.

Assistance being extended by the Agriculture, Forestry, and Fisheries Ministry to promote biotechnology and other high technology research in the nation is not confined to budgetary and material support. The ministry has been offering technological backing through joint research with private-sector institutions. The ministry is involved in joint research with Mitsubishi Chemical Industries, Ltd., to develop the regeneration technology of rice through cell fusion. With Kikkoman Corp. the ministry has launched another joint research project to create a new plant through cell fusion between the ordinary orange and trifoliate orange. Among other joint research projects in which the ministry is involved are some in which promising research results are beginning to emerge.

In Japan, the rights of the developer of a new plant is protected doubly by the Agriculture, Forestry, and Fisheries Ministry's Seeds and Saplings Law, and the Ministry of International Trade and Industry's Patent Law. The provisions in the Seeds and Saplings Law prohibit: 1) the production of seeds and saplings of plants registered under the law for the purpose of making money; 2) the sale of cut flowers grown using such seeds or saplings; and 3) the sale of seeds of the F1 species (the first filial generation) which has been bred using the registered species of a plant as its parent.

The rights of the developer of an officially registered new plant are also protected internationally under the provisions of the UPOV (Union Internationale Pour la Protection des Obtentions Vegetabes) treaty. Under the treaty, the developer's rights are protected for 15 years. This treaty allows for the seeds of domestically registered plants to be exported to foreign countries with the rights of the developers protected in those countries just as in the exporting country.

The only problem in Japan concerning the patent issue involving newly developed plants is the difference in the extent of the developer's rights to be protected under the two relevant laws--the Patent Law and the Seeds and Saplings Law.

Under the Seeds and Saplings Law, persons may freely harvest seeds from the plants they have planted, even though the plants in question are officially

registered. But the Patent Law does not permit such practice. So under the law, people who plant some of those registered plants for harvesting seeds must pay royalties to the developer every year when they do so.

It is undeniable that under the Patent Law, the rights of the developers are better protected. But there also are disadvantages with the stricter Patent Law. First, under the law, there are cases in which farmers must pay royalties every year even when they are exempted from royalty obligation under the Seeds and Saplings Law. Second, when the protection of the developers' rights under the Patent Law is enforced as strictly as the law originally stipulated domestically, there can arise concern that nursery firms in Europe and the United States, where the rights of the developers of new plants are not protected by their patent laws, will come into the Japanese market seeking the benefits of the Japanese law.

One disputed case which emerged in connection with the extent of production by these two separate domestic laws in question is the case of a new species of mugwort developed by Nippon Shinyaku Co., Ltd. The mugwort species contains a high content of santonin, a substance effective in killing intestinal worms.

After an application by the pharmaceutical firm was filed with the government office for official recognition and the protection of the firm's rights over the species as the developer, the Ministry of International Trade and Industry's Patent Office was planning to grant protection under the Patent Law when the Ministry of Agriculture, Forestry, and Fisheries raised an objection to the Patent Office's move. The later ministry's argument was that if the office granted protection under the Patent Law it would result in violating the UPOV treaty, which bans duplicate protection of the developer of a new plant. The ministry also opposed the Patent Office's move in view of avoiding two-tiered administration concerning the plant patent. The dispute between the two governmental departments was settled in June this year (1985).

The contents of the agreement are as follows: 1) the rights of the developer of a new plant species are protected under the Seeds and Saplings Law; 2) the Patent Law is invoked when the methods used to develop a new species of plant involve biotechnology; and 3) the rights of Nippon Shinyaku Co., Ltd., over the new species of mugwort should be protected under the Patent Law because the firm's application came before the Seeds and Saplings Law was enforced in December 1978 and prior to Japan's signing of the UPOV treaty in February 1977. The firm made an application for a patent for the mugwort species in February 1977, but prior to the signing of the treaty in the same month.

In recent years, two noteworthy trends or developments have emerged in the plant seed business and the biotechnology involving the development of new plants. First, private-sector seed firms in the country have been accelerating their efforts to acquire stocks in leading foreign concerns in similar businesses and to establish joint ventures with them in their domestic business activities. Domestic seed firms have also been recommending organization into groups by admitting firms even from outside the industry. Second, it is a noteworthy development that the major Sumitomo Chemical Co., Ltd., has joined

other smaller domestic seed business firms in filing an application for official recognition of a species of rice which the company developed.

Biotechnology Research in Agricultural Field

Firm names	Remarks
Kirin Brewery Co., Ltd.	Has a business tieup with Plant Genetic of the United States in the joint development of artificial plant seeds. Has established technology for the sterile culturing of seed potatoes on its own.
Kikkoman Corp.	In cooperation with the Ministry of Agriculture, Forestry, and Fisheries, the firm has succeeded in developing a new plant species through fusion of the cells of the ordinary orange and trifoliate orange.
Kagome Co., Ltd.	Far ahead of other firms in the number of official registration of new breeds of tomatoes. Studying the possibility of exporting hybrid tomatoes.
Nichirei Corp.	Has started research on cell fusion involving potato and other plants at its subsidiary Agrogenetic Corp. In cooperation with a French firm, Nichirei has started volume production of orchids through tissue cultivation.
Mitsui Toatsu Chemicals, Inc.	As of July this year (1985), the company had filed applications for official registration for four species of plants, including carrot and pumpkin, since the start of the year. Besides these, the firm is preparing to make many more applications for official registration.
Sumitomo Chemical Co., Ltd.	Has a business tieup with Rohm & Haas Co. of the United States in developing the F1 plant of rice. Has filed applications for official recognition of newly developed breeds of rice plants jointly with other domestic firms.
Mitsubishi Chemical Industries Ltd.	In cooperation with the Ministry of Agriculture, Forestry, and Fisheries, the firm started research on cell fusion and the regeneration of rice plants. Has set up a research lab with Mitsubishi Corp.
Kyowa Hakko Kogyo Co., Ltd.	Ahead of other firms in the technology for tissue cultivation of gold-banded lily. In addition, has succeded in establishing the technology for volume production of hyacinth and strawberries.

Until around 1983, the activities of the major domestic seed companies listed on the stock exchange had been confined to a relatively small scale. Their activities included investments in smaller seed business firms, formation of industrial groups to strengthen cooperation among the member firms, and business tieups. As examples of leading firms investing or participating in the business of traditional seed firms are investments by Mitsubishi Corp. and Mitsubishi Yuka Fine Chemicals Co., Ltd., in Kyowa Shubyo Co., Ltd., and by Sumitomo Chemical Co., Ltd., and Sumitomo Corp. in Yamato Shubyo Ryokuka Co., Ltd. As to the formation of groups, Mitsui Toatsu Chemicals, Inc. joined hands with Mitsui Petrochemical Industries, Ltd., to strengthen technical cooperation between the two companies. Mitsubishi Corp. and Mitsubishi Chemical Industries Ltd. made joint investments to set up the Plant Engineering Research Laboratory. As a business tieup between the two top-class firms, there is a case between Mitsubishi Corp. and Takii & Co., Ltd.

Beginning around 1984, the moves among domestic seed business-related firms to form groups, acquire stocks in foreign firms, and establish joint ventures have gained momentum. In addition, cooperation between the public and private sector has accelerated for conducting joint R&D.

Under these circumstances, Sumitomo Chemical Co., Ltd., established a tieup with Rohm & Haas Co. of the United States in developing the F1 species of rice plants. In addition, Kirin Brewery Co., Ltd., signed a contract with the U.S. venture corporation Plant Genetics for the joint development of artificial plant seeds. Meanwhile, a cooperation system between the public sector and the private-sector business companies was established between the Ministry of Agriculture, Forestry, and Fisheries and two major firms--Kikkoman Corp. and Mitsubishi Chemical Industries Ltd.

In the biotechnological research to develop new plants and produce seeds, those stock exchange-listed firms involved in the business have achieved steady progress in their research activities.

In 1981, there were five new registered plants of corporates listed on the stock exchange and their affiliated companies. But the number continued to increase to 6 in 1982, 7 in 1983, and 15 in 1984. In 1985 the number of registered plants has already reached 14 as of the end of July. Especially noteworthy among those firms which have succeeded in developing new plants is Sumitomo Chemical Co., Ltd., which conducted joint research with a local agronomist in Hiroshima to develop a new species of rice. Sumitomo filed a joint application with the Hiroshima man to have their newly developed rice species officially recognized. At last, the efforts of private-sector firms have begun to bear fruit in their research to develop principal agricultural plants.

The following are the typical items which have been chosen from among many new products, plants, and other achievements made by domestic companies in biotechnological research. In the agricultural chemical field, there are BT agricultural chemicals developed by Sumitomo Chemical Co., Ltd., and Toagosei Chemical Industry Co., Ltd., and a herbicide trade-named Herbiace developed by Meiji Seika Kaisha, Ltd.

In the field of tissue cultivation, research involves gold-banded lily and hyacinth by Kyowa Hakko Kogyo Co., Ltd., ginseng by Nitto Electric Industrial Co., Ltd., production of shikonin from gromwell by Mitsui Petrochemical Industries, Ltd., mass production of an orchid species by Nichirei Corp., sterile cultivation of seed potatoes by Kirin Brewery Co., Ltd., and extraction of red pigment from Euphorbia by Nippon Paint Co., Ltd.

In the field of bioreactors and cell fusion, there is Aspartame by Ajinomoto Co., Inc., L-phenylalanine by Denki Kagaku Kogyo K.K., fusion and cultivation of the protoplast of rice by Mitsubishi Chemical Industries Ltd., and the fusion of the cells of the ordinary orange and trifolate orange by Kikkoman Corp.

Bioagricultural Chemicals: Most Effective With Side Effects Minimal

Enormous Global Market for Herbicides--Concerted Efforts for Diversification of Developmental Methods

Freely Using Multiphased Methods

Together with pharmaceutical goods, agricultural chemicals are typical fine chemical products. The use of chemicals in agricultural crops is the most effective way to protect the crops from harmful insects and crop diseases. It is said that if no agricultural chemicals were used, the harvest would drop 20 to 30 percent. Although agricultural chemicals are one of the indispensable items in food production, the performance of Japanese corporations specializing in manufacturing agricultural chemicals has been deteriorating rapidly.

This plight for the industry has resulted partly from the makers' shipping their products at substantially low prices in recent years, which they were forced to do because of the special merchandise distribution system in the industry and partly from the difficulties they are experiencing in developing new farm-use chemicals. In spite of these difficulties, domestic makers are continuing positive efforts to develop new products, including the development of new agricultural chemicals using biotechnology. High hopes are placed on the results of efforts to develop new farm chemicals using biotechnology. The current market of agricultural chemicals in Japan is about ¥350 billion. This compares with the world market of ¥4 trillion, more than 10 times larger than the domestic market. Considering the size of world markets, the possibility is strong that domestic makers' successful development of new agricultural chemicals, including biotechnology products, in the future could lead to a steep increase in exports of those chemicals to foreign markets.

Therefore, many domestic manufacturers, chiefly major producers, are strongly interested in developing new agricultural chemicals using biotechnology. The appeal of biotechnology-based farm chemicals lies in the fact that such chemicals allow an increase of agricultural production without destroying the natural environment. Agricultural chemicals which are being developed by domestic makers using biotechnology make use of various biotechnological elements to produce the chemicals, ranging from bacteria, nematodes and hormones to activate substances produced by the plant itself.

Behind the popularity of the biotechnology-based agricultural chemicals, in addition to their relative safety, is the promising potential of biotechnology, which has attracted strong attention in the industry as a form of high technology in recent years. Biotechnology is a technology being used in producing useful chemical and other substances by making use of the functions of formation and metabolism, which bacteria have. There is no established definition for the so-called bioagricultural chemicals. But bioagricultural chemicals are taken generally to represent the agricultural chemicals which have been produced using bacteria and the substances produced by those creatures. The chemicals are aimed at adversely affecting the life mechanism of harmful insects and weeds so as not to have to rely on traditional natural enemies to protect agricultural crops. Expectations of biotechnology-based agricultural chemicals are high with regard to reducing the levels of residual poisonous substances of traditional organically synthesized agricultural chemicals in farmland and their harmful side effects on domestic animals, birds, and fish in rivers.

The research results of those companies engaged in the development of new agricultural chemicals were presented at a forum of the Japan Agricultural Chemistry Society held in late July this year (1985) at Hokkaido University in Sapporo. Among the results presented, the new agricultural chemicals developed using biotechnology drew the particular attention of the audience. In August the same year, the Agricultural Chemical and Biotechnology Research and Development Union, which began research activities in fiscal 1984, also gave its research results along with its forecast on the direction the industry would take in biotechnology-related activities in the coming years. The organization was established to develop new agricultural chemicals using biotechnology and is participated in by 16 firms. The organization is headed by Nobuo Soh, president of Hokko Chemical Industry Co., Ltd.

In the forecast, the organization said that agricultural chemicals developed using biotechnology will become the ideal farm chemicals of the future and will have higher effectiveness than conventional ones and fewer adverse side effects. The forecast also says that the introduction of biotechnology into agricultural chemical production may bring about a change in the character of the chemicals, and at the same time may cause a revolution in the production method of agricultural chemicals.

Japan is experienced in the development of antibiotics for agricultural applications. (Polynactin), a type of antibiotic developed for killing mites, and (biolaphos), another type of antibiotic for use in herbicides, both developed for agricultural use, are produced using Antinomyces. They were developed using the expertise which the nation's microorganism industry accumulated through its research. The existence of this established industrial foundation has enabled Japanese researchers to display their competence in the development of BT and plant growth chemicals, all derived from bacteria, in coming years.

In contrast with the progress made so far in the development of agricultural chemicals using bacteria, almost no significant progress has been made in the application of the physiological activation substances derived from higher plants. But nicotine contained in tobacco and pyrethrin in Dalmatian pyrethrum

has been used as insecticide for many years, and they have been useful substances as research materials in drug design.

The multiplication speed of the cells of higher animals and plants is slower than that of microorganisms and this makes them unsuitable for industrial use as the production vehicle of biotechnological products. Rather the usefulness of the cells of those higher animals and plants is to use them as materials in research for obtaining new substances for use in fighting viruses, insects, and nematodes, and for obtaining new plant hormones by raising or cultivating those animals and plants or their cells.

With the recent progress in biotechnological research, researchers are trying to make use of the inherent resistivity of plants against plant diseases to develop new agricultural chemicals. So far, no attempts have been made to exploit the self-protective mechanism of plants to make agricultural chemicals because of high production costs involved and low activation levels of the reaction. But in the future, with further progress in biotechnological research, it may become possible to enhance the activation level.

As described so far, active research is underway in the biotechnological industry in Japan aimed at developing new agricultural chemicals using the technology. Using biotechnology, researchers are trying to develop new farm chemicals with fewer harmful side effects and to increase output in the production of agricultural chemicals. By achieving these goals, biotechnology research activities of the nation's business concerns and other research institutions will gain further momentum in the future.

The business concerns which are in the forefront of the efforts to develop new agricultural chemicals using biotechnology are Meiji Seika Kaisha, Ltd., Toagosei Chemical Industry Co., Ltd., and Shin-Etsu Chemical Co., Ltd.

In July 1984, Meiji Seika put a herbicide on the market containing an antibiotic produced using an Actinomyces called Streptomyces hygroscopicus as the main ingredient. Cell fusion techniques were used to prompt the Actinomyces to produce the antibiotic.

This biotechnology-based herbicide is trade-named Meiji Herbiace. The main ingredient of the agricultural chemical is (biolaphos), an antibiotic produced by Streptomyces hygroscopicus. The antibiotic, when used against plants, hinders the metabolism of nitrogen in them and this causes them to wither. The herbicide has proved effective on every type of weeds.

The process Meiji Seika employed to obtain the Streptomyces hygroscopicus is as follows. The company found that there are two types of microorganisms prior to obtaining the Actinomyces. One is a type which has a high ability to decompose bialaphos, and another is a type which has a low productive capability of the antibiotic but its ability to decompose it is also low. Researchers at the company removed the cell walls from each of these microorganism strains to obtain the protoplasts. Then, they were put together in a receptacle containing PEG (polyethylene glycol) as a cell fusion accelerator. Then follows the process of cell fusion.

The process concludes with choosing the most appropriate type from among the hybrid strains of cells created by the fusion, which has the highest productivity of bialaphos but exhibits the lowest power of decomposition. Then the chosen strain of the hybrid cells is allowed to multiply to facilitate the production of bialaphos in volume. In the future, a continual progression in biotechnological research in the field of agricultural chemicals will make it possible to produce bialaphos using other microorganisms, such as colon bacilli, using the gene recombination method.

Among agricultural chemicals, the international markets for herbicide are particularly large. In the future, biotechnology-based herbicide is expected to grow into a major farm chemical product and its sales on the international markets is expected to increase sharply.

Prior to Meiji Seika Kaisha, Ltd., Toagosei Chemical Industry Co., Ltd., began marketing an insecticide which contains a toxin produced by Bacillus Thuringiensis (called BT bacteria) in the spring of 1983. The toxin is contained in the crystalline proteins produced by the microorganism. The insecticide is effective only on the Lepidoptera family of creatures, including the green caterpillars and moths which feed on vegetables and leaf folders which damage apples.

In addition to the Toagosei Chemical Industry Co., Ltd., Sumitomo Chemical Co., Ltd., also markets biotechnologically produced agricultural chemicals using the BT bacteria. These companies are continuing biotechnological research aimed at increasing productivity in manufacturing their agricultural chemicals by, for example, introducing the gene which controls the generation of the crystalline proteins in colon bacilli instead of using the actinomycetes.

Another company, Shin-Etsu Chemical Co., Ltd., started marketing a pheromone-based insecticide called Hamakikon in April this year (1985). Since then, industry people have begun to show increased interest in developments related to pheromone as an effective element in producing insecticides. So far, four kinds of pheromone-based insecticides have been officially registered as agricultural chemicals. They are Pherodin SL and Shinkui-con of Takeda Chemical Industries, Ltd., and Gatori Hoihoi of Earth Chemical Co., Ltd., besides the Hamakikon of Shin-Etsu Chemical.

Hamakikon is a chemically synthesized version of the odorous pheromone which female insects excrete from their bodies during their mating season. Hamakikon as an insecticide is contained in a polyethylene tube dispenser measuring about 20 cm long with a diameter of 5 mm which is placed at various locations in the fields. Male insects are unable to find the whereabouts of the females and this limits the multiplication of harmful insects. Hamakikon is particularly effective for use among tea plants since it limits the regeneration of insects belonging to the leaf folder family which damage the plant.

According to a report, the U.S. Department of Agriculture started testing Shin-Etsu Chemical's pheromone insecticide at cotton farms in California in May this year (1985). If good results are obtained in the experimental use in the United States, there is a strong possibility that the market of the

company's insecticides could expand to the cotton growing regions of the world in the future.

In recent years, Sumitomo Chemical Co., Ltd., a major agricultural chemical manufacturer in Japan, has also stepped up its efforts to develop biotechnology-based farm chemicals. The principal substance involved in this company's R&D effort is a hormone excreted by caterpillars or larvae as young insects. The excretion levels of this hormone begin to drop when the time to become adult insects approaches, so it is possible to prevent those young insects from becoming adults by artificially administering large amounts of the hormone to them. It is said that Sumitomo Chemical is preparing to file an application in the coming few years to have its syntheiszed hormone officially recognized as an insecticide.

Since June 1984, Nippon Kayaku Co., Ltd., has been engaged in research to apply nematodes to the development of insecticide by importing the creature from an Australian biotechnology venture company, Biotechnology Australia. Asahi Chemical Industry Co., Ltd., has discovered a substance which can weaken the activation level of superoxidedismutase (a type of enzyme commonly called SOD for short), and this opened the way for the company to develop a biotechnological herbicide. The enzyme plays an important role within the body of living organisms.

Meanwhile Suntory Ltd. has announced that it has succeeded in extracting a useful chemical compound from seaweed which the company claims is effective in killing harmful creatures. As described so far in this chapter, many domestic firms are engaged in brisk research activities in an effort to develop new agricultural chemicals using biotechnology.

Biotechnology Agricultural Chemicals and Developers

Firm names	Remarks
Toagosei Chemical Industry Co., Ltd.	In the spring of 1983 began marketing insecticide Toarow CT wettable powder which the firm developed using BT bacteria.
Meiji Seika Kaisha, Ltd.	In July 1984 began marketing a herbicide trade-named Herbiace, which the firm developed using an antibody generated by actinomycetes. Also engaged in research to develop agricultural chemicals using gene recombination techniques.
Shin-Etsu Chemical Co., Ltd.	Began marketing an insecticide trade-named Hamakikon in March 1985. The insecticide uses a pheromone as the ingredient which obstructs insect males from locating their female partners for pairing.

[continued]

[Continuation of Biotechnology Agricultural Chemicals and Developers]

Firm names	Remarks
Sumitomo Chemical Co., Ltd.	Is expected to file an application for official registration of its newly developed insecticide in 1988. The substance to be used in the insecticide prevents young insects from becoming adults. Also engaged in basic research to develop a new germicide utilizing those microorganisms which have symbiotic relationships with certain plants.
Nippon Kayaku Co., Ltd.	Is engaged in the development of a new insecticide using a nematode which the firm imports from an Australian company. At present, the insecticide is tested to evaluate its effectiveness by actual use in farm fields.
Asahi Chemical Industry Co., Ltd.	Engaged in basic research for developing a new herbicide by making use of a substance which obstructs SOD in plants.
Suntory Ltd.	Engaged in basic research for developing a new insecticide which makes use of a substance extracted from seaweed.

In developing those agricultural chemicals, the methods and the kinds of weeds and creatures against which the chemicals are designed for use differ widely from company to company. In the future, a company which succeeds in developing a major agricultural chemical using biotechnology, which has a higher safety factor and greater effectiveness and ease of use, may control the agricultural chemical market. The successful development of such a product greatly contributes to boosting the profits of the developer.

Chemical Field: World's Top Level Stationary Technology

Commercialization of Bioreactor Technique in Chemical/Foods Field

World's First Operation in General-Purpose Petrochemical Field

In August 1985 the world's first bioreactor facility in the commodity petrochemical field went into operation in Japan. It is a bioreactor facility for producing acrylic amide built and run by Nitto Chemical Industry Co., Ltd.

Bioreactor is a technology which facilitates the manufacture of chemical substances by enhancing various chemical reactions involved in their efficient production and using enzymes and bacteria as the catalysts. When a conventional production facility is used, producing those chemical substances requires large-scale facilities which consume much energy and the production

process involves high temperatures and high pressures. The use of bioreactor permits the production of these substances at room temperature and ordinary atmospheric pressure conditions, enabling the producer to conserve energy and other resources.

To put it more plainly, bioreactor is a technology for applying the natural biochemical reactions taking place within plants and the bodies of living creatures to industrial applications outside the plants and the bodies of those creatures.

Inside the human body, the digestion of food, absorption of nutrients from the food and metabolism, all vital activities to sustain human life, are taking place with the aid of various kinds of enzymes present inside the body. Bioreactor is a technology to make those same biochemical reactions which take place inside a human body realized outside the body, artificially.

While attempting human body biochemical reactions outside the body, the cost of maintaining the reaction could be substantial if the living organism catalysts are discarded after every round of reactions is over and must be recovered for reuse or a new dosage of the catalysts must be added to compensate for the loss. This is why the technology to immobilize the catalysts becomes necessary so they can be used repeatedly and continuously.

Japan leads the world in fixation technology. Tanabe Seiyaku Co., Ltd., was the first in the world to utilize the enzyme fixation technology in practical industrial applications and to produce commercial products using the technology. In 1969 the pharmaceutical company succeeded in immobilizing the aminoacyl acid hydrolysis enzyme and produced L amino acid using DL amino acid as the material. The company succeeded in putting bioreactor technology into practical application more than 10 years before the term "bioreactor" began to be used popularly.

As well as Tanabe Seiyaku, there are already a few companies in Japan which have put the technology into practical application. They include Snow Brand Milk Products Co., Ltd., and Ajinomoto Co., Inc. But the fields of applications in most of those firms are confined to food products. Through the production of Japanese sake, soysauce, and miso, all of these being traditional fermented Japanese food items, Japanese firms have had fundamental bioreactor technologies cultivated in their long experience of producing these food items for many years. This background is believed behind Japan's position today as the world leader in bioreactor technology, particularly in the field of food production.

Outside the food manufacturing field, there have been few instances of success in practical applications of bioreactor technology in the world. In the field of commodity chemicals, such as the production of acrylic amide, it has long been the dream of petrochemical industry people of the world to produce such items using bioreactor technology.

The acrylic amide is used for increasing the strength of paper as a water treatment agent and for improving farmland soils. The chemical was produced

Bioreactor Research Themes and Participating Food Industry Firms

Themes	Participating firms
Production of starch sugar	Oji Corn Starch, Mitsui Seito K.K., Komatsugawa Koki, Ishikawa Seisaku
Production of alpha cyclodextrin	Ensuito, Nippon Organon K.K., Showa Sangyo Co., Ltd., Nitto Electric Industrial Co., Ltd., Nikken Chemicals Co., Ltd.,
Production of sugar substances for moisture activation adjustment	Suntory Ltd., New Japan Chemical Co., Ltd., Hitachi Zosen Corp.
Production of oligosaccharide	Nissin Food Products Co., Ltd., Kirin Brewery Co., Ltd., Chiyoda Chemical Engineering & Construction Co., Ltd., Yokogawa Hokushin Electric Corp.
Production of heteroligosaccharide	Meiji Seika Kaisha, Ltd., Shimazu
Production of food materials from wheat gluten	Nisshin Flour Milling Co., Ltd., Koboko, Mitsubishi Heavy Industries, Ltd.
Development of new food products based on liquid nutrients extracted from beans	Kyodo Nugyo, Toyo Jozo Co., Ltd., Mitsui Shipbuilding & Engineering Co., Ltd.
Production of functional proteins (soybean)	Fujiyu, Amano Pharmaceutical Co., Ltd., Kakoki
Production machine of functional proteins (milk)	Snow Brand Milk Products Co., Ltd., Amano Pharmaceutical Co., Ltd., Iwai Kikai Kogyo, Toyobo Co., Ltd.
Production of functional proteins (blood)	Prima Meat Packers, Ltd., Toyo Jozo Co., Ltd., Kurita Water Industries Ltd.
Decomposition of the proteins of fish	Yaizu Suisan Kagaku Kogyo, Wakamoto Pharmaceutical Co., Ltd., Soga Seisakusho
Decomposition of various protein materials	Kikkoman Corp., Kurita Water Industries Ltd.
Production of soysauce	Shoda Shoyu, Koboko, Nisshin Engineering
Production of seasoning and flavoring	Sanbishi Co., Ltd., Amano Pharmaceutical Co., Ltd., Nippon Saryo Seizo Kaisha, Ltd.
Production of high-density vinegar using aerobic fermentation method	Q.P. Corp., Komatsugawa Kakoki
Production of symmetry triglyceride	Asahi Denka Kogyo K.K., Meito Sangyo Co., Ltd., Kakoki

[continued]

[Continuation of Bioreactor Research Themes and Participating Food Industry Firms]

Themes	Participating firms
Adding of functionality to edible oil and fat	Ajinomoto Co., Inc., Amano Pharmaceutical Co., Ltd., Nikki Chemical Co., Ltd.
Improvement of soybean lecithin	Yakult Honsha Co., Ltd., Niigata Engineering Co., Ltd.
Development of meat flavors	Ito Ham Provisions Co., Ltd., Hasegawa Koryo, Unitika Ltd., Shibaura Engineering Works Co., Ltd.
Production of food materials based on fish oil	Toyo Jozo Co., Ltd., Nippon Oils & Fats Co., Ltd., Sanki Engineering Co., Ltd.

Source: Ministry of Agriculture, Forestry, and Fisheries

for the first time by Nitto Chemical Industry Co., Ltd., using the sulfuric acid catalytic method. But the method was much costlier than the copper catalytic method which came into use later. Nitto Chemical has managed to maintain its market share for the chemical by receiving valuable assistance from other companies in the industry.

The microorganism catalytic method, or bioreactor method, follows the copper method. If the sulfuric acid catalytic method and copper catalytic method can be called the first and second generation catalytic method, respectively, then the bioreactor method can be regarded as the third generation method.

The advantages of the microorganism method are: 1) energy conservation because the reactions take place at room temperature and ordinary atmospheric pressure and 2) lower costs in building plant facilities. The only drawback is the necessity for extra energy for condensing the obtained acrylic amide because the density of the product made using the microorganism catalytic method is thin. But despite this necessity, it is said that overall production costs in a facility using the bioreactor method is 20 to 30 percent cheaper than the cases using conventional methods.

By introducing the bioreactor techniques, Nitto Chemical Industry is again able to produce the acrylic amide from acrylonitrile on its own without assistance from other firms in the industry. Recently, an acrylic amide production plant having a production capacity of 4,000 tons per year started operating at the company. Industry observers are keeping watch over the developments in the operation of the plant and will continue to do so in the future because the plant introduced bioreactor technology into the nation's petrochemical industry.

Many domestic chemical firms have been deeply involved in biotechnology by now. The names of the 10 companies as listed on the following page along with their activities in biotechnological R&D are only a small portion of

Ten Major Chemical Firms Involved in Biotechnology Research

Firm names	Remarks
Mitsui Toatsu Chemicals, Inc.	Places emphasis on research in the field of agriculture such as the efforts to develop hybrids of rice plant.
Nitto Chemical Industry Co., Ltd.	Has succeeded in putting bioreactor technique into practical use for the first time in the world in the field of producing commodity petrochemical goods.
Sumitomo Chemical Co., Ltd.	Has accumulated substantial expertise in research in the fields of plant breeding and agricultural chemicals.
Mitsubishi Chemical Industries Ltd.	Engaged in research covering a wide field and centering on medical and agricultural fields. The level of the results of the research is high.
Kyowa Hakko Kogyo Co., Ltd.	Enjoys high reputation in research related to biomass. Has achieved good results in research covering the pharmaceutical, fishery, and agricultural fields.
Mitsui Petrochemical Industries, Ltd.	Has achieved good results in the field of tissue cultivation as shown by the firm's success in putting shikonin into practical application.
Japan Synthetic Rubber Co., Ltd.	Engaged in research for developing monoclonal diagnostic medicines at Immunis Co., Ltd., a subsidiary of the firm.
Nippon Zeon Co., Ltd.	Has achieved good results in research for DNA synthesis. Engaged in joint research with the People's Republic of China in tissue cultivation.
Nippon Oils & Fats Co., Ltd.	Has achieved good results in research for developing fatty acids using bioreactor technology. Engaged in research to unravel the mechanism of senility.
Kao Corp.	Engaged in research on tissue cultivation, bioreactor, and development of biotechnology chips.

those chemical firms. But compared with the situation in food and medical product manufacturing industries, the number of instances of biotechnological application to practical purposes is still small in the chemical industry. This is because, at present, the efforts of those chemical firms involved in biotechnology are directed chiefly at the development of high value-added products like agricultural chemicals and pharmaceutical items, and this inevitably makes them divert fewer resources to the development of commodity chemical products.

However, with further progress in biotechnology, it is expected that the instances of application of the technology to the production of other kinds of chemical goods on a commercial basis will increase gradually in the future. In the course of the progress in biotechnology research and the technology's application to practical purposes, the bioreactor technology will play the key role.

The four points which must be tackled in the course of bioreactor R&D efforts are as follows: The first is the necessity to search for sources of the genes utilized for developing useful enzymes and bacteria. A second is the necessity to establish the technology for volume production of those useful enzymes and bacteria. A third point concerns the fixation of enzymes and bacteria. The last point concerns the technology to separate an intended substance from less useful substances and condense the obtained product. In Japan, the basic technology needed to implement these processes is being established. The introduction of bioreactor technology into manufacturing plants may take place gradually starting with part of the process on the production line. But in the end, the use of bioreactor techniques may spread to the entire production process.

Another major theme which must be tackled in pushing ahead with the biotechnology research is to produce fine chemical products using tissue cultivation and cell fusion technologies. With further progress in the research, it may become possible in the future to switch from the present petroleum-based materials to natural plants to produce goods and improve productivity further.

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REPORT ON NEW MATERIALS, RELATED DEVELOPMENTS

Tokyo NIKKO MATERIALS in Japanese Apr 86 pp 23-29

[Text] Ceramics

Oxygen Atmosphere HIP Unit for Molding Oxide Ceramics

MHI (Mitsubishi Heavy Industries, Ltd.) has developed an oxygen atmosphere HIP (hot isostatic pressing) unit for molding oxide ceramics such as alumina, etc., in collaboration with Toray Industries, Inc. Deteriorating and tarnishing cracks can be prevented by adding oxygen gas to an inactive gas used as a pressure medium. These deteriorating and tarnishing cracks are caused by oxide ceramics while using the oxygen atmosphere HIP unit.

This unit is designed to pressure-sinter powder at a high temperature of 1,000 to 2,000 degrees centigrade and at high pressure of 1,000 to 2,000 kilograms per cubic centimeter, densify the sintered powder, and remove internal defects.

When molded ceramic products were pressure-sintered using the HIP unit, they deteriorated due to insufficient oxygen. For this reason, the following method is used. Oxygen gas is added to inactive gas used as a pressure medium.

However, it was difficult to put oxide ceramics to practical use because the use of oxygen gas in furnaces at high temperature and pressure may cause an explosion. Thanks to the HIP unit developed by the MHI, it is possible to use oxygen gas at a high temperature of 1,400 to 1,500 degrees centigrade by adopting special metal, ceramics, etc., as materials for controlling systems and heating furnaces. Oxide ceramics are widely used in magnetic heads, semiconductor materials, medical members, etc. It is expected that this development will sharply enhance the quality and function of oxide ceramics.

Crystalline Glass Which Can Be Casted and Machined Is Used as a Material for Chemical Plants

Ishihara Chemical Co., Ltd. will import a crystalline glass, "Ilmavit 40" from an East German company, and will put it on the market.

Ilmavit 40 can be casted and machined. Features of the ILMAVIT 40 are as follows: 1) The main crystal of the crystalline glass is mica; 2) the glass has a structure with a density close to that of casting surfaces because it is a casted product; 3) the glass can be readily machined, i.e., turned, milled, and drilled with general tools and machine tools. In addition, the glass has excellent heat resistance, electrical insulating properties, heat insulating properties, corrosion resistance, aging resistance, and dimensional stability. Primarily, it is expected that the glass will be used as a material in chemical plants because it is more resistant to concentrated sulfuric acid than high-grade alloy steel. The glass is nontoxic to the human body, lightweight, and can be mass produced. It is also anticipated that crystalline glass can be used as a heat resisting material or an insulating material.

The main specifications are as follows: 1) The density is 2.7 grams per cubic centimeter at a temperature of 20 degrees centigrade; 2) the maximum allowable working temperature (critical temperature at which any creep is not generated under load) is 800 degrees centigrade; 3) the thermal conductivity is 0.0022 calories per centimeter second degrees centigrade; 4) volume resistivity is 2×10^{11} ohm-centimeters; 5) the coefficient of thermal expansion (20 to 200 degrees centigrade) is 104×10^{-7} per degrees centigrade.

The company carries out the casting and machine work for the glass on the basis of the user's design, and delivers the glass to the users. It is possible for the company to deliver both on-specification products and machined products.

Lion Akzo and Mitsubishi Petrochemical Jointly Establish a New Company Which Will Manufacture Electroconductive Carbon

Lion Akzo Co., Ltd. and Mitsubishi Petrochemical Co., Ltd. have jointly established a new company, Ketjen Black International Co., Ltd. in order to develop an electroconductive carbon business. The new company pioneered the business.

Both companies have taken productive action since they established the "Japan EC Co., Ltd." in 1979 so they could domestically produce an electroconductive carbon black, Ketjen Black EC (brand name) whose technology was introduced by Akzo Chemie BV. in Holland. They have established the new company in order to expand their business.

The electroconductive carbon is widely used in IC (integrated circuit) packages, toner for copying machines, magnetic tapes, etc. It is expected that this carbon will be used increasingly in various fields in the future. Recently, Mitsubishi Petrochemical Co., Ltd. has developed the EC-DJ600 (also known as supergrade) by using its own technology. Particularly, the EC-DJ600 has three times the electroconductivity of conventional products, and its charged samples are evaluated highly. Therefore, the company has decided to radically extend the electroconductive carbon business and integrate its

production and sales. Although the investment ratio of the company to Japan EC Co., Ltd. was 10 percent, that of the new company is 33.4 percent.

The new company will take over the Mitsubishi Petrochemical Yokkaichi Facility with an annual production capacity of 800 tons as a production base from Japan EC Co., Ltd., and will increase the annual production capacity to 1,400 tons by 1987. The sales of electroconductive carbon in Southeast Asia and Japan will be under the auspices of Lion Akzo Co., Ltd. and Mitsubishi Petrochemical Co., Ltd., and in the United States will be under the auspices of Akzo Chemie BV. After Japan EC Co., Ltd. transfers its assets and business to the new company, it will take the necessary steps for dissolution.

Also, in the near future, Akzo Chemie BV. will close its electroconductive carbon plant which has an annual production capacity of 500 tons, presently in operation in Ireland, and will centralize the production base into the new plant.

The new company's capital is Y50 million. The investment ratio of Lion Akzo Co., Ltd. is 66.6 percent, and that of Mitsubishi Petrochemical Co., Ltd. is 33.4 percent. The headquarter's address is, Lion Ryogoku Bldg. 2-22, Yokoami 1-chome, Sumida-ku, Tokyo. Itsumi Yumane, managing director of Lion Akzo Co., Ltd. will be inaugurated as president of the new company.

High-Hardness Fine Ceramics Ground with Ultrasonic Waves at High Speed

SPC Electronic Corp. and Osaka Diamond Industrial Co., Ltd. have developed a grinding machine in cooperation with Assistant Professor Kuniaki Umino at the Vocational Training College. This grinding machine can grind high-hardness fine ceramics such as silicon nitride, silicon carbide, etc., with ultrasonic waves at a speed 5 to 10 times that of conventional grinding machines.

The new machine is designed so a diamond-bonded grinding wheel rotating at high speed combines with the longitudinal vibration generated from ultrasonic waves. It efficiently grinds hard and brittle ceramics by using a composite effect of rotation and vibration. The surface of these fine ceramics is very smooth, and there is no concern about surface cracks. Also, it is possible for the new machine to cope with special requirements, because the outside diameter of a diamond-bonded grinding wheel tool tip can be changed from several millimeters to 6 centimeters. In addition, the new machine can carry out three-dimensional work such as simple drilling work, grooving work, etc., because it is interlocked with an NC (numerical control) unit.

Both companies expect that personnel expenses, which account for 80 percent of the fine ceramic manufacturing cost, can be sharply reduced.

The price of the new machine made by SPC Electronic Corp. is Y28 million, and that made by Osaka Diamond Industrial Co., Ltd. is Y19 million. The former machine is slightly larger than the latter.

The Strength of Machinable Ceramic Based on Aluminum Nitride Is Equivalent to That of Alumina

Tokuyama Soda Co., Ltd. has developed a machinable ceramic based on aluminum nitride, Shapal M (brand name). This machinable ceramic has strength equivalent to that of alumina and can be drilled, cut, etc., in the same way as metallic materials.

The company has succeeded in developing machinable ceramics using translucent aluminum nitride manufacturing technology developed under the leadership of Professor Shigekazu Udagawa at Tokyo Institute of Technology, Engineering Department, Inorganic Material School, and Professor Yoshitaroh Yoshida at the University of Chiba, Engineering Department, Mechanical School. The bending strength of the machinable ceramic is about 30 kilograms per square millimeter, which is equivalent to that of alumina. The machinable ceramic has about five times the thermal conductivity of alumina.

Generally speaking, fine ceramics have excellent strength and heat resistance, but they have the disadvantage of being difficult to work with because they are hard and brittle. For this reason, machinable ceramics are being developed by adjusting manufacturing methods. But, there is a tendency for the original characteristics to be lowered in proportion to the degree of rise in workability. The bending strength of fine ceramics with good workability was less than 10 kilograms per square millimeter.

The company has already completed a pilot plant in the Development Division of Fujisawa Research Institute located in Fujisawa-shi, Kanagawa-ken, and has started shipping samples of structural materials to various fields.

C. Itoh Participates in the Field of Ceramics by Establishing a New Company

C. Itoh & Co., Ltd. has established a company specializing in ceramics sales as a general trading company on 21 January.

That is: C. Itoh & Co., Ltd. established this independent company as a ceramic division with plans to participate in the field of new ceramics such as silicon, etc., whose demand will definitely increase. The name of the new company is C. Itoh Ceramics Co., Ltd. The new company will engage engineers and develop new ceramics. It is a subsidiary company, fully owned by C. Itoh & Co., Ltd.

Its capital is Y80 million. Tadao Okumura, manager of Ceramic Mineral Product Department of C. Itoh & Co., Ltd. will be inaugurated as president of the new company, which will begin business on 1 April. The new company will aim sales proceeds of Y15 billion in the first fiscal year, and is scheduled to increase sales proceeds to Y20 billion 3 years later. The new company will consist of 20 employees, including 2 or 3 experts and 9 employees transferred from C. Itoh & Co., Ltd. The number of employees will increase gradually.

Metals

Fatigue Test Time for Metallic Materials Reduced to One-Tenth

The RDCJ (Research Development Corp. of Japan) has developed a high-level repeated material tester which can reduce the fatigue test time for metallic materials to one-tenth the conventional time. The RDCJ had commissioned Akashi Seisakusho, Ltd. to put this tester to practical use.

It is said to be possible to conduct tensile-compression tests with a load of 6 tons and a maximum of 160 cycles per second. The tester is designed so that measuring methods such as the ultrasonic flaw detecting method, etc., could be used during repeated-tests. Also, data on occurrence and growth of cracks could be obtained.

The standard number of repeated cycles of fatigue tests for steel, etc., is said to be about 10 million, but depending on materials and environment, 100 million to 1 billion fatigue test cycles may be required. Thanks to the use of the new tester, it is possible to take a repeating speed figure up one place, reduce the fatigue test time, and carefully conduct tests.

The basic technology was developed by Assistant Professor Teruo Kishi, et al. at the University of Tokyo, Faculty of Engineering, Institute of Interdisciplinary Research.

Very Thin (Thickness of 20 MM) Speaker Unit

Sawafuji Dynameca Co., Ltd. has developed a very thin (thickness of 20 millimeters) plane wave full range overall driving type speaker unit, the DP-F18.

The basic structure and operation principle of this speaker unit are the same as those of its sister, the DP-12. Compared with the same class speaker units, the DP-F18 has excellent sound quality, because of its high sound pressure level and its extended aperture. In addition, it possesses the following features: 1) High-magnetic flux density, high-endurance, high-sensitivity, high-durability, and high-vibration strength can be obtained by strictly checking materials; 2) strain and resonance can be removed due to the completely uniform driving system; and 3) the adoption of circular rear sound holes can prevent magnetic leakage.

The regenerative frequency band is 50 to 22,000 hertz, the impedance is 6 ohms, the output sound pressure level is 87 decibels per watt-meter, the size is 222 x 186 x 20 millimeters, and the weight is 1 kilogram.

The company will prepare products which meet user's needs, and aim at spreading the new speaker unit throughout the interior, the housing industry, the public facility industry, etc., and fields other than acoustics.

KSC Establishes a New Company To Produce Magnets in Collaboration with Pechiney in France

KSC (Kawasaki Steel Corp.) has established a joint corporation in collaboration with Aimants Ugimag S.A., a subsidiary of Pechiney, a non-ferrous metal company nationalized in France. This joint corporation will produce permanent magnets in Japan.

The name of the new company is Nihon Ugimag Corp. The initial capital is Y800 million. It will increase its capital to Y4.5 billion in 3 years. The investment rate for both KSC and Pechiney is 50 percent. On 10 February the new company held a meeting, and Jun-ichiroh Tsuboi, leader of the Ugimag Project Team of KSC was named president.

The reason KSC has decided to branch out into the field of magnets is that it believes the magnet market will expand in accordance with the growth of the electronics industry. KSC manufactures iron oxide and calcined powder, which are the raw materials for ferrite, and markets them. KSC has decided to introduce technology from Aimants Ugimag S.A., which represents a magnet manufacturer in Europe, because KSC is in a good position to obtain raw materials.

The new company will begin constructing a plant at Chonan-cho, Chosei-gun, Chiba-Ken this spring. The plant will begin operations in the autumn of 1987. First the plant is planning to produce ferrite magnets at a monthly production rate of 220 tons, while gradually increasing the amount and types produced. The new company is scheduled to invest about Y10 billion in the plant over 4 years, and aims at obtaining annual proceeds of Y10 billion by the fifth year of operation. When the plant starts operations, the number of employees will be 170 to 180, with a scheduled increase to 400 in 5 years.

Magnetic Filter Extracts Magnetically Suspended Particles Contained in Water

IHI (Ishikawajima-Harima Heavy Industries Co., Ltd.) has developed a magnetic filter employing permanent magnets and magnetic stainless particles in cooperation with Toshiba Corp. and Nippon Yakin Kogyo Co., Ltd.

This magnetic filter is designed so it can magnetize stainless particles around the inside of its cylinders with permanent magnets, and it can extract, and remove magnetically suspended particles such as rust contained in water.

At present, the decrease of clads contained in cooling water has become an important problem for nuclear power plants because the radiation exposure rate must be lowered. Also, supercritical pressure boiler sections of thermoelectric power plants have a problem in that scales adhering to the piping inside, etc., exfoliate in water, adhere to the inside of boiler heat transfer pipes and cause a decrease in thermal efficiency. Magnetic filters have been adopted with the intention of solving these problems.

But, it is necessary to provide a power supply and water cooling facilities necessary for the generation of magnetic fields. The magnetic filter developed by IHI does not need any coil for generating magnetic fields, because a permanent magnet is used in the magnetic filter.

In addition, it possesses the following features: 1) It can be used even in the event of a power supply interruption or water supply suspension; 2) plants can be readily operated and maintained if the magnetic filter is used in these plants; 3) it is possible to uniformly extract, catch, and filter sludge in deep layers; 4) it can be used at high temperatures.

High-Heat Resistant Alloy Made of Ceramics and Metallic Composite Materials Used in Rollers for Hot Rolling Work

Mitsubishi Metal Corp. has developed a high-heat resistant alloy, and has marketed it. This high-heat resistant alloy has 5 to 10 times the toughness of conventional high-speed steel.

The steel and metallic rolling industries that need hot rolling work, require a lengthened life span for the rollers used. There is a tendency for hard metal rollers to be used instead of conventional cast steel at the finishing and intermediate rolling processes. But, hard metal has the disadvantage of not being as tough as steel.

The new material is made by adding 5 to 20 percent high-hardness ceramic powder based on titanium nitride and titanium carbide to the powder of high-speed steel. That is, it is made by adopting the powder metallurgy method, and is said to be a composite material having both wear resistance and toughness. When using the new material for rollers in the hot rolling mills, those employing the new material have 7 to 10 times the life span of conventional rollers employing cast steel. In the case of thread rolling dyes, up until now it has been possible to cut only 800 threads, but it has become possible to cut more than 4,000 threads.

When considering the price of rollers, the new material cost is 10 percent lower than that of hard metal. The company is planning to disperse the new material throughout the rolling and molding industries, tool manufacturers, etc.

Composite Material for High-Precision Instruments Made by Coating Ceramics With High-Strength Cast Iron

Hitachi Shipbuilding & Engineering Co., Ltd. has developed a composite material, LEC (brand name) made by coating ceramics with high-strength cast iron, and has marketed it. The LEC is used for high-precision instruments. It is made by adding the high-hardness of ceramics to cast iron with a low-thermal expansion and high-damping capacity.

This cast iron has been developed independently by Hitachi. The company has already developed the LE.LEN cast iron for high-precision instruments, and has

marketed it. This LE.LEN cast iron consists of iron, manganese, silicon, etc., with a nickel base. It is coated by spraying it with plasma or by physiochemical deposition, etc.

The LE.LEN cast iron has about one-third the thermal expansion coefficient and about twice the damping capacity of conventional gray cast iron.

The company has made plans to conduct research on the composition of cast iron and ethylene trifluoride, and will concentrate on the development of new composite materials in the future.

Plastics

Transparent, Conductive, and Cleaning Film Used in Semiconductor and Biochemical Fields

Showa Denko K.K. has developed a packaging material in collaboration with Nippon CIC Research Corp. This packaging material is used in a clean room to carry and store clothing, equipment, materials, etc.

Showa Denko K.K. has developed a transparent, conductive, and cleaning film, Clearstat (brand name) using no antistatic agents. But Clearstat has an antistatic effect. Nippon CIC Research Corp. has developed a cleaning and packaging system using ultrapure water in clean rooms, and has marketed it under the name SSC Bag.

The antistatic effect is produced on Clearstat by coating the surface with an oxide substance. Clearstat is made from L-LDPE (linear-low density polyethylene) or PP (polypropylene) as a raw material. The SSC Bag is manufactured by cleaning, drying, and packaging the Clearstat original negative in a clean room.

Features of the SSC Bag are as follows: 1) The contents and the inside of clean rooms are not contaminated because the inside of the SSC Bag is clean and an antistatic agent was not used in the Clearstat; 2) the SSC Bag has excellent transparency and conductivity; 3) the SSC Bag encounters no problems from static electricity.

The price of roll films with a width of 300 millimeters and a length of 20 meters is Y16,800, and a set of 100 300-millimeters-square bags is Y35,000.

High-Heat Resistant Aramid Fiber Is Mass Produced

Unitika Ltd. has developed a meta base aramid fiber, Apyeil (brand name) in collaboration with Nippon Aroma Co., Ltd., and plans to mass produce it in the near future. Apyeil can withstand a temperature of 400 degrees centigrade.

The aramid fiber is classified into two types, i.e., meta base and para base, depending on its molecular structure. The product developed by both companies is a meta base aramid fiber having high-heat resistance as its most important

feature. Du Pont E.I. de Nemours & Co. in the United States and Teijin Limited have individually developed fibers, and have controlled equally the market up to now. This market has increased sharply in proportion to the increase in fibers used for such items as industrial materials and clothing.

The new product is manufactured by directly spinning aromatic polyamide in which molecular chains can be readily crystallized at reaction temperatures suitable for spinning work. This new product possesses the following features: 1) It can withstand high-temperatures of 400 degrees centigrade; 2) it has excellent flame-retardant qualities, dimensional stability, acid resistance, and chemical resistance. Although conventional fiber thickness is 1.5 to 2 deniers (thickness per gram of a fiber of 9,000 meters), new fiber thickness is 0.5 to 1 denier. These new fibers are extremely thin and have conductivity.

Both companies are planning to increase the fiber demand for flameproof clothes and various heat-resistant and insulating materials. Nippon Aroma Co., Ltd. has completed a facility with an annual production capacity of 100 tons at the Nippon Aroma Okazaki Plant, and will increase the annual production capacity to 200 tons in the spring of 1987.

Ceramics Plasma-Sprayed on Plastics

Mitsubishi Rayon Co., Ltd. has developed a technology for lightly spraying fine ceramics on the surface of plastics using an ultra-high-temperature plasma spray coating method, in collaboration with Professor Yoshiaki Arata (chief of Welding Engineering Research Institute) at Osaka University. The company will start taking orders and producing.

The plasma spray coating method was used when ceramics coat metallic surfaces, but it was impossible to use this method on plastics, because of the ultra-high temperatures needed. For this reason, the company has developed a surface structure with momentary high-heat resistance in which ceramics will adhere to each other, by applying a special inorganic material to the surface of plastics and by a special pretreatment to which acrylic resin manufacturing technology is applied. Thanks to this surface structure, it has become possible to use the plasma spray coating method at a temperature of 20,000 degrees centigrade.

Plastics used as matrices are composites of carbon fiber and EP (epoxy resin) and various high-function resins such as MMA (methyl methacrylate) resin, ABS (acrylonitrile-butadiene-styrene) resin, etc. Fine ceramics such as alumina, titanium oxide, cobalt oxide, etc., are sprayed on these moldings, and ceramic granules with a thickness of 0.1 to 0.3 millimeters are bonded to the moldings.

The new composite material possesses the following features: 1) It is lightweight (equal to that of plastic); 2) it has high moldability and high impact resistance; 3) the surface hardness is about twice that of steel; 4) it is hard to flaw; 5) the momentary melting point is as high as 1,500 to 2,500

degrees centigrade; 6) the molding cost is equal to the cost of plating plastics. This new composite material is used for fishing rods, golf club heads, high-speed rotating rollers, etc.

Integral Molding of Conductive Layers--Electromagnetic Wave Shielding Method Employing Static Electricity

Dai Nippon Toryo Co., Ltd. has developed a new material, Metalfilm, for shielding electromagnetic waves and a new process, TNS, in collaboration with Tokai Kogyo Co., Ltd., and has started putting them to practical use.

The Metalfilm is encapsulated by a thin surface coating of metalic powder such as nickel, copper, etc., with acrylic resin, etc. Although the Metalfilm shows insulation properties in a powdery condition, when it is applied to plastics by using the injection molding method, it will become electrically conductive. The TNS method means that the Metalfilm is applied to metallic molds of injection molding machines by using static electricity, and conductive layers are formed in the inside and outside of molded products by injection-molding of the plastics.

Conductive paint has been applied to the injection-molded plastics until now to shield the electromagnetic waves. But, the new technology is used to simultaneously shield the electromagnetic waves and injection-mold the plastics. This new technology has the following features: 1) The work time can be sharply shortened; 2) the coating efficiency has been enhanced from 15 to 20, to 50 to 60 percent because static electricity is used to apply the Metalfilm to the metallic molds; 3) there is neither precipitation nor separation; 4) it has high stability and workability; 5) formed layers are very smooth, because they are compressed with molding faces; 6) there is no anxiety about electrical shorts caused by the dropping of metallic powder.

Dai Nippon Toryo Co., Ltd. estimates that the total cost of the new technology can be reduced to half that of conventional methods, and is planning to integrate its use throughout the areas of microcomputers, connectors, electric appliance housing, etc.

Decorative Unsaturated Polyester Laminate With Extremely High-Fungus Resistance

Dainippon Ink & Chemicals, Inc. has developed a decorative unsaturated polyester laminate, Dic-Shine BC (brand name) which is effective in retarding the growth of funguses on the surface of decorative laminates.

The Dic-Shine BC is manufactured by combining the unsaturated polyester, Polylite and heat resistant fungus retardent agent Biocut, and affixing this to plywood using a film method. Also, both Polylite and Biocut have been developed by the company. There is relatively little generation and propagation of funguses on decorative unsaturated polyester laminates using the film method, because the resin film layer is thick compared with that of

decorative laminates manufactured by fixing resin impregnated papers to plywood with pressure.

However, the generation of funguses on the surface of decorative laminates cannot be prevented under high-temperatures and high-humidity. With regard to the new decorative laminate, the effectiveness of fungus retardants has increased sharply while maintaining the physical properties of decorative unsaturated polyester laminates using the conventional film method.

Results of a fungus resistance test (test pieces of the new and conventional decorative laminates are left for 90 days at a temperature of about 28 degrees centigrade), funguses were generated on more than 50 percent of the conventional test pieces, but on less than 10 percent of the new ones. The fungus retardant agent used in this test is barely soluble in water, and is extremely stable, because the melting point is 150 degrees centigrade and the decomposition point is 300 degrees centigrade. In addition, the effectiveness of fungus retardants can be maintained over a long period of time because the agent is uniformly dispersed in the resin.

The price is about 10 percent higher than that of conventional decorative laminates. But, the new decorative laminate is suitable as a wall covering for water piping systems of kitchens, bathrooms, etc.

Metal Coating to CFRP Roll

Mitsubishi Rayon Co., Ltd. has developed a metal coat (hard chrome) processing technology to CFRP (carbon fiber-glass reinforced plastics).

Previously, it was difficult to carry out the coating treatment of CFRP on the surface of carbon fibers, and particularly when the CFRP was used in CFRP rolls the powder of carbon fibers would be scattered into the air.

The company has developed a surface treatment agent to solve this problem. This surface treatment agent is used to raise adhesive properties of the boundary surface between CFRP and metal. It has become possible to carry out the hard chrome treatment by using the surface treatment agent.

Thanks to this technology, the metal-coated CFRP roll possesses the following features: 1) It is lightweight, about 60 percent of the aluminum roll with the same diameter and modulus of longitudinal elasticity; 2) the moment of inertia is small; 3) it has a small mechanical loss generated from power such as motor, etc., to rolls; 4) dimensional accuracy is high, being equal to metallic rolls; 5) low noise; 6) excellent durability and stability.

The company is planning to adopt the technology involving rolls of low-inertial rotors, high-speed rotors, etc.

High-Frequency Absorbing Film With an Absorption Coefficient of 80 to 90 Percent

Daishin Co., Ltd. has developed a high-frequency absorbing film, Electronic Microwave Control Film (brand name), and will start marketing it in the near future. The Electronic Microwave Control Film can efficiently absorb high-frequencies of 2 to 14 gigahertz oscillated from radar equipment, etc.

This new film is manufactured by filling fillers based on special ceramics in plasticized urethane vinyl chloride resins. The reflection absorption coefficient of conventional film materials is 20 to 40 percent, while the new film is 80 to 90 percent. Also, the new film has excellent heat and cold resistance, from minus 40 to 160 degrees centigrade.

The new film is available in three standard types with thicknesses of 100, 150, and 200 microns. An overcoat layer of 25 microns is added to all of the new films. First the company will produce and market the 100 micron film (one roll . 1,040 millimeters x 400 meters). The estimated price is Y16,000 per meter.

The company will export the new film for nuclear shielding work to the United States through a joint concern, Daishin USA, which will be established in California in the middle of February. In other words, the company is planning to market the new film by exporting it to foreign countries.

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NUCLEAR DEVELOPMENT

FACILITY UTILIZATION RATIO FOR JUNE REPORTED

Tokyo GENSHIRYOKU SANGYO SHIMBUN in Japanese 3 Jul 86 p 8

[Text] The actual operating record of nuclear power generating plants (including "Fugen") was 84.4 percent facility utilization ratio and 83.1 percent uptime. In April and May of 1986, the facility utilization was around 70 percent but the ratio has since gone up to 80 percent.

The reason is that, in June, no new regular inspection was in progress or scheduled. In April, there was a total of 11 generating units under regular inspection, and 4 units in May. In June there were also 4 units under regular inspection; namely, Tokai No 2 (BWR [boiling water reactor], 1.1 million kW), Mihama No 2 of Kansai Electric (PWR [pressurized water reactor], 500,000 kW), Takahama No 2 (PWR, 870,000 kW), and Shimane of Chokoku Electric (BWR, 460,000 kW).

The facility utilization ratio according to the reactor type was: 16 BWR units (total output of 12,917,000 kW) average 82.7 percent; 15 PWR units (total output of 11,438,000 kW) average 86.1 percent; 1 GCR [gas cooled reactor] unit 79.7 percent; and 1 ATR [advanced thermal converter reactor] unit 100 percent.

The average facility utilization ratio according to utility company was: Tokyo Electric Power 90.8 percent (10 units, 9,096,000 kW); Kansai Electric Power 78.5 percent (9 units, 7,408,000 kW); Kyushu Electric Power 100 percent (4 units, 2,898,000 kW); Chubu Electric Power 97.9 percent (2 units, 1,380,000 kW); and Shikoku Electric Power 100 percent (2 units, 1,032,000 kW).

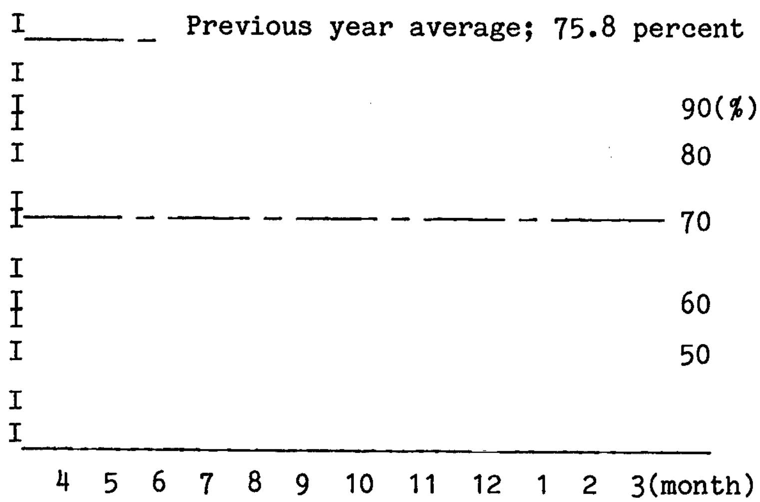
There are 13 power generating units which are operating at 100 percent facility utilization in individual generating station basis, and, also, there are 11 units which operated at almost 100 percent facility utilization ratio. All in all, the ratio was about 80 percent.

$$\text{Facility utilization} = \frac{\text{Amount of power generated}}{\text{Certified output x total elapsed time}} \times 100\%$$

$$\text{Uptime} = \frac{\text{Power generating time}}{\text{Total elapsed time}} \times 100\%$$

Average facility utilization ratio

(dotted line; previous year average)



Facility utilization according to reactor type

	Units	Output, 10,000 kW	Facility utilization, percent
BWR	16	1,291.7	82.7
PWR	15	1,143.8	86.1
GCR	1	16.6	79.9
ATR	1	16.5	100.0
Total	33	2.468.6	84.4

Facility utilization according to utility company

Company	Units	Output, 10,000kW	Facility utilization,%
Nihon Atomic Energy	3	162.3	64.1
Tohoku	1	52.4	0
Tokyo	10	909.6	90.8
Chubu	2	138.0	97.9
Kansai	9	740.8	78.5
Chukoku	1	46.0	35.4
Shikoku	2	113.2	100
Kyushu	4	289.8	100
(Fugen)	(1)	(16.5)	100

(1) **原子力発電所の運転速報 6月**（原産調べ）

	(2)発電所名	(3)型式	(4)認可出力 (万kW)	(5)時間稼働率 (7)稼働時間 (H)	(%)	(6)設備利用率 (8)発電電力量 (MWH)	(%)	(9)備考
(10)	東海	GCR	16.6	720	100	95.506	79.9	
(11)	東海第二	BWR	110.0	636	88.3	654.080	82.6	第7回定検中(1.20～)(6.4併入) (30)
(12)	敦賀1	〃	35.7	0	0	0	0	第16回定検中(5.16～) (31)
(13)	女川	〃	52.4	0	0	0	0	第2回定検中(4.19～) (32)
(14)	福島第一・1	〃	46.0	720	100	325.261	98.2	
	〃 2	〃	78.4	720	100	564.480	100	
	〃 3	〃	78.4	720	100	564.480	100	
	〃 4	〃	78.4	720	100	556.359	98.6	
	〃 5	〃	78.4	0	0	0	0	第7回定検中(4.20～) (33)
	〃 6	〃	110.0	720	100	792.000	100	
(15)	福島第二・1	〃	110.0	720	100	792.000	100	
	〃 2	〃	110.0	720	100	792.000	100	
	〃 3	〃	110.0	720	100	776.830	98.1	
(16)	柏崎・刈羽1	〃	110.0	720	100	783.900	99.0	
(17)	浜岡1	〃	54.0	720	100	388.651	100	
	〃 2	〃	84.0	720	100	583.618	96.5	
(18)	美浜1	PWR	34.0	720	100	244.563	99.9	
	〃 2	〃	50.0	490	68.1	213.241	59.2	第10回定検中(4.2～)(6.10併入) (34)
	〃 3	〃	82.6	720	100	590.911	99.4	
(19)	高浜1	〃	82.6	720	100	594.634	100	
	〃 2	〃	82.6	0	0	0	0	第8回定検中(3.28～) (35)
	〃 3	〃	87.0	720	100	626.375	100	
	〃 4	〃	87.0	343	47.6	245.925	39.3	第1回定検中(4.7～)(6.16併入) (36)
(20)	大飯1	〃	117.5	720	100	845.590	100	
	〃 2	〃	117.5	720	100	825.945	97.6	
(21)	島根	BWR	46.0	282	39.2	117.277	35.4	第11回定検中(1.9～)(6.19併入) (37)
(22)	伊方1	PWR	56.6	720	100	407.311	99.9	
	〃 2	〃	56.6	720	100	407.332	100	
(23)	玄海1	〃	55.9	720	100	402.238	99.9	
	〃 2	〃	55.9	720	100	402.316	100	
(24)	川内1	〃	89.0	720	100	640.701	100	
	〃 2	〃	89.0	720	100	640.400	99.9	
(25)	小計または平均		2.452.1	19.031	82.6	14.873.924	84.2	
(26)	(カッコ内は前月)		(2.452.1)	(16.513)	(69.4)	(12.728.757)	(69.8)	
(27)	ふげん	ATR	16.5	720	100	118.800	100	
(28)	合計または平均		2.468.6	19.751	83.1	14.992.724	84.4	
(29)	(カッコ内は前月)		(2.468.6)	(17.257)	(70.3)	(12.844.165)	(69.9	

Key:

1. Current status of nuclear power generation in July (surveyed by Japan Atomic Industrial Forum)
2. Name of power station
3. Types of reactors
4. Certified output (10,000 kW)
5. Uptime
6. Utility utilization ratio
7. Operating time (hour)
8. Power output (MWh)
9. Remarks
10. Tokai
11. Tokai 2
12. Atsuruga 1
13. Onagawa
14. Fukushima No. 1; 1
15. Fukushima No. 2; 1
16. Kashiwazaki.Kariba 1
17. Hamaoka 1
18. Mihama 1
19. Takahama 1
20. Oi 1
21. Shimane
22. Ikata 1
23. Genkai 1
24. Kawauchi 1
25. Subtotal or average
26. Data of previous month
27. Fugen
28. Total or average
29. Data of previous month
30. Under the seventh inspection (since 20 January) (integrated on 4 June)
31. Under the sixteenth inspection (since 14 May)
32. Under the second inspection (since 19 April)
33. Under the seventh inspection (since 20 April)
34. Under the tenth inspection (since 2 April) (integrated on 10 June)
35. Under the eighth inspection (since 28 March)
36. Under the first inspection (since 7 April) (integrated on 16 June)
37. Under the eleventh inspection (since 9 January) (integrated on 19 June)

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END

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